

FIG. 1

FIG. 2A

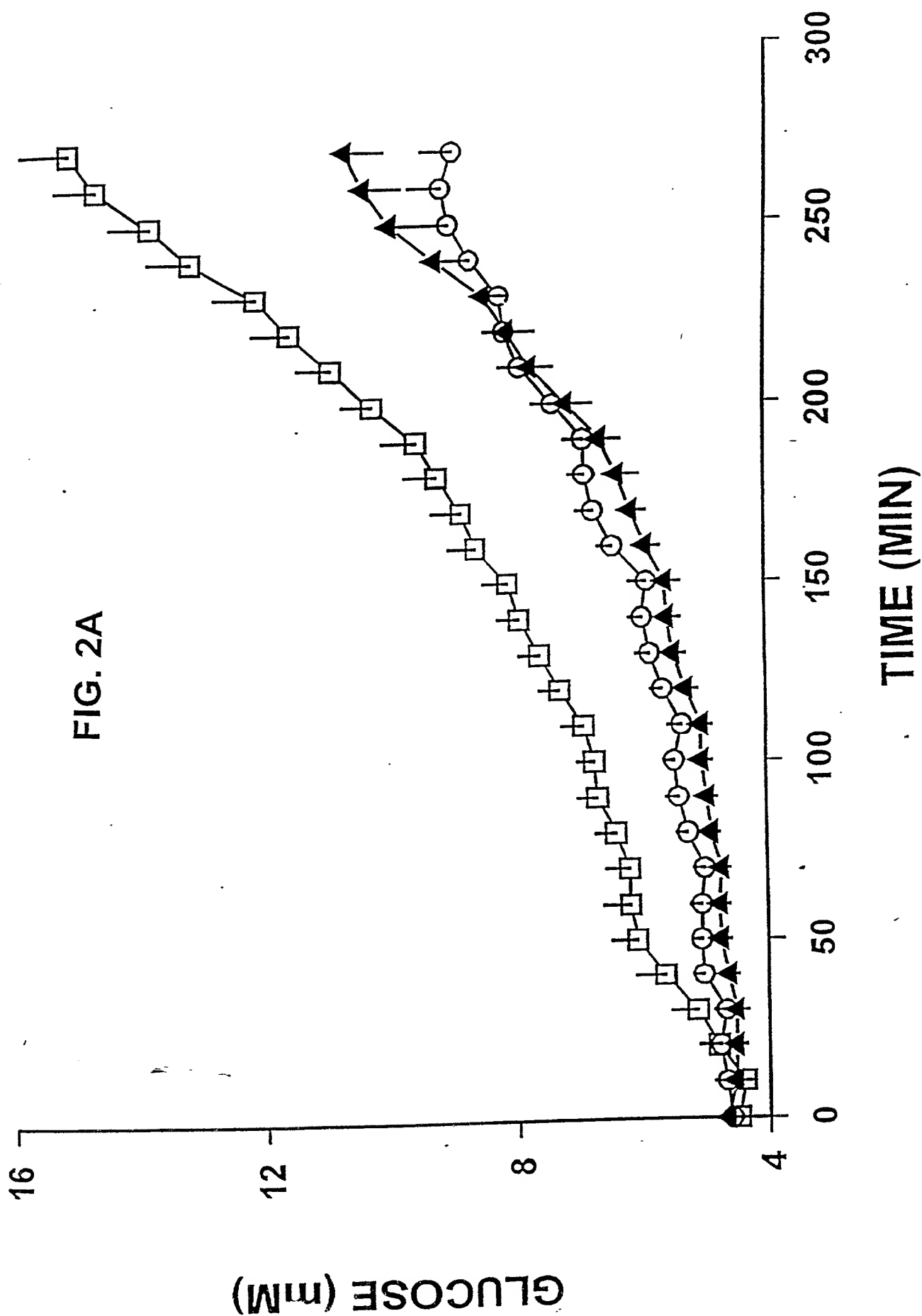


FIG. 2B

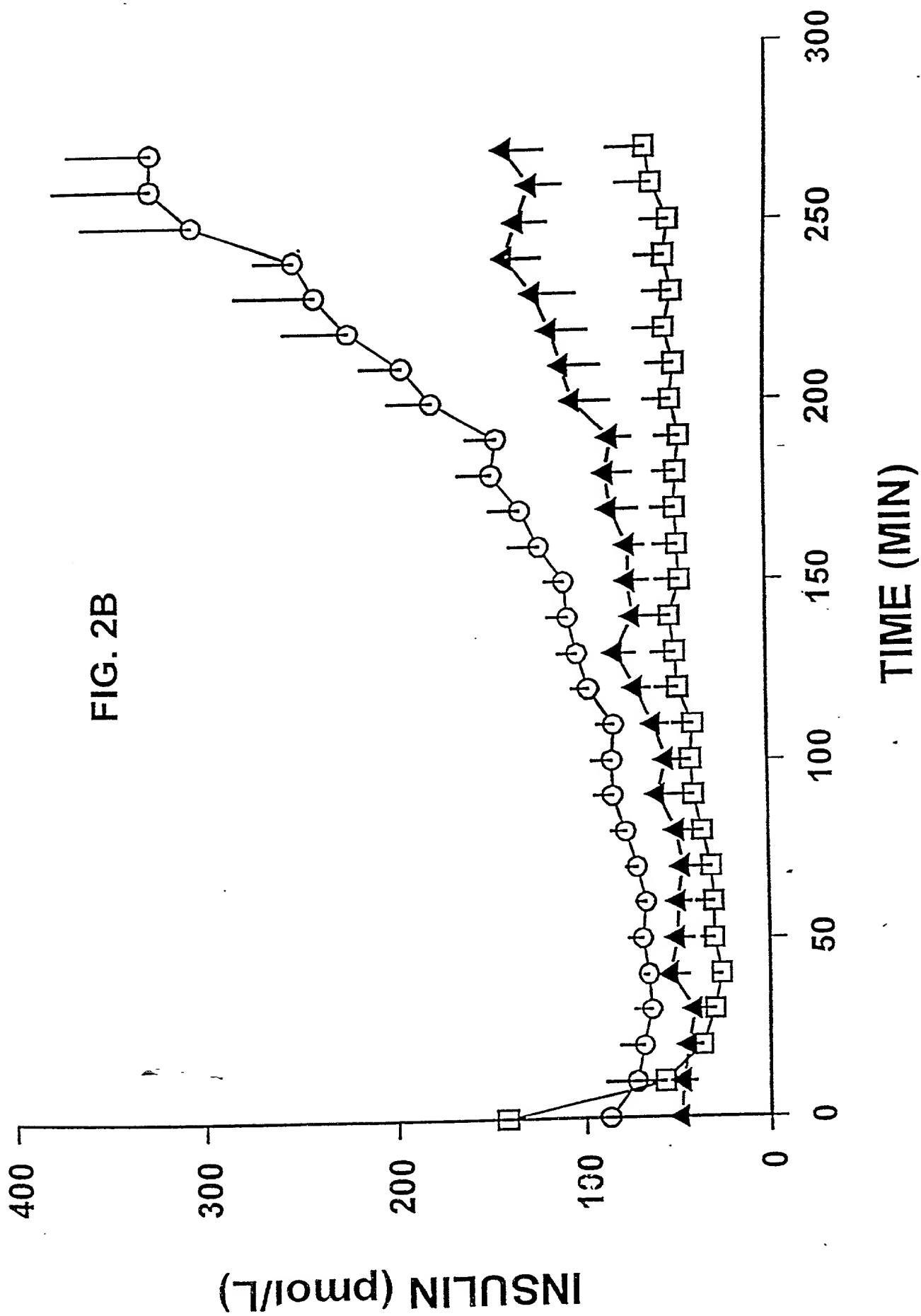
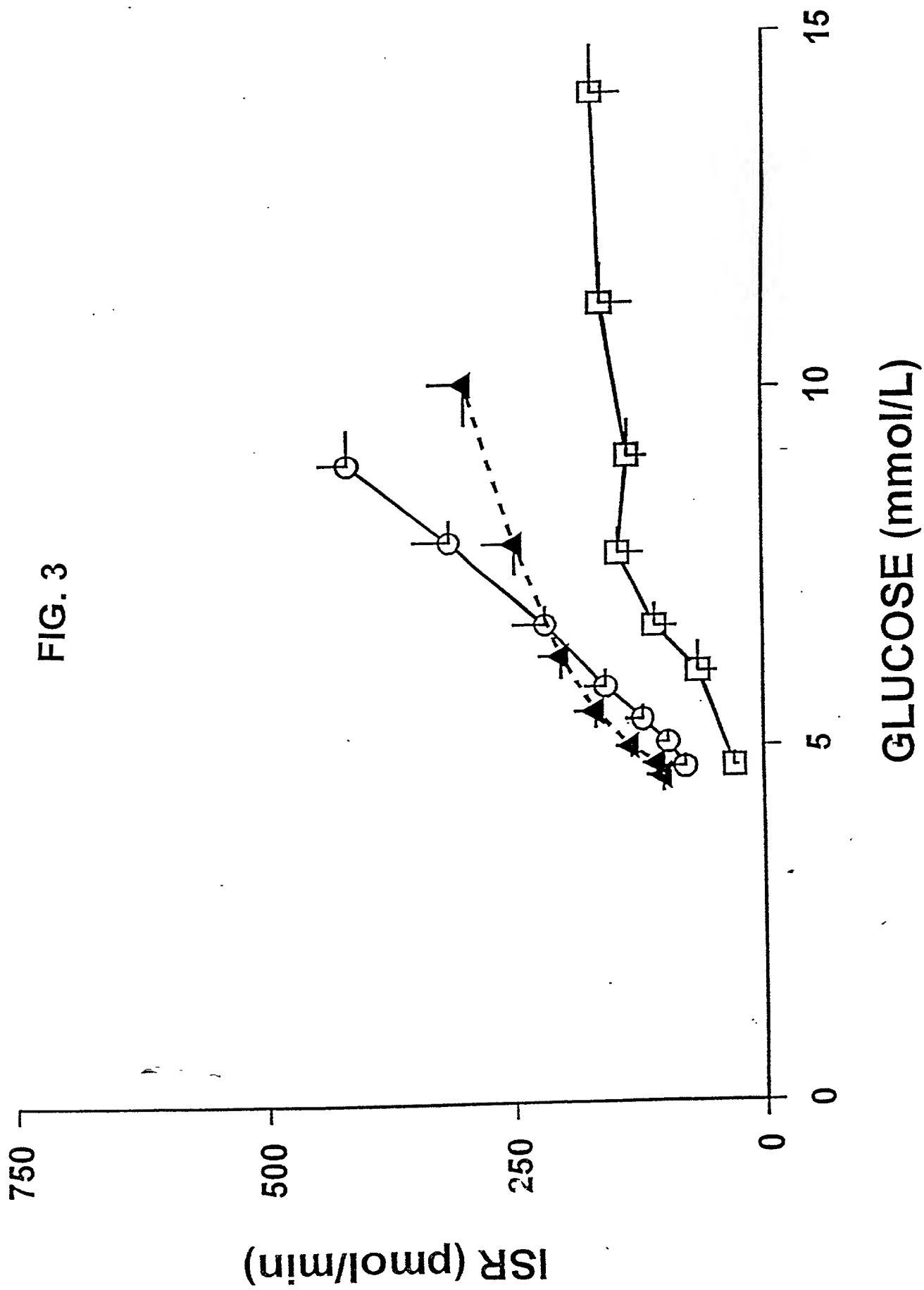
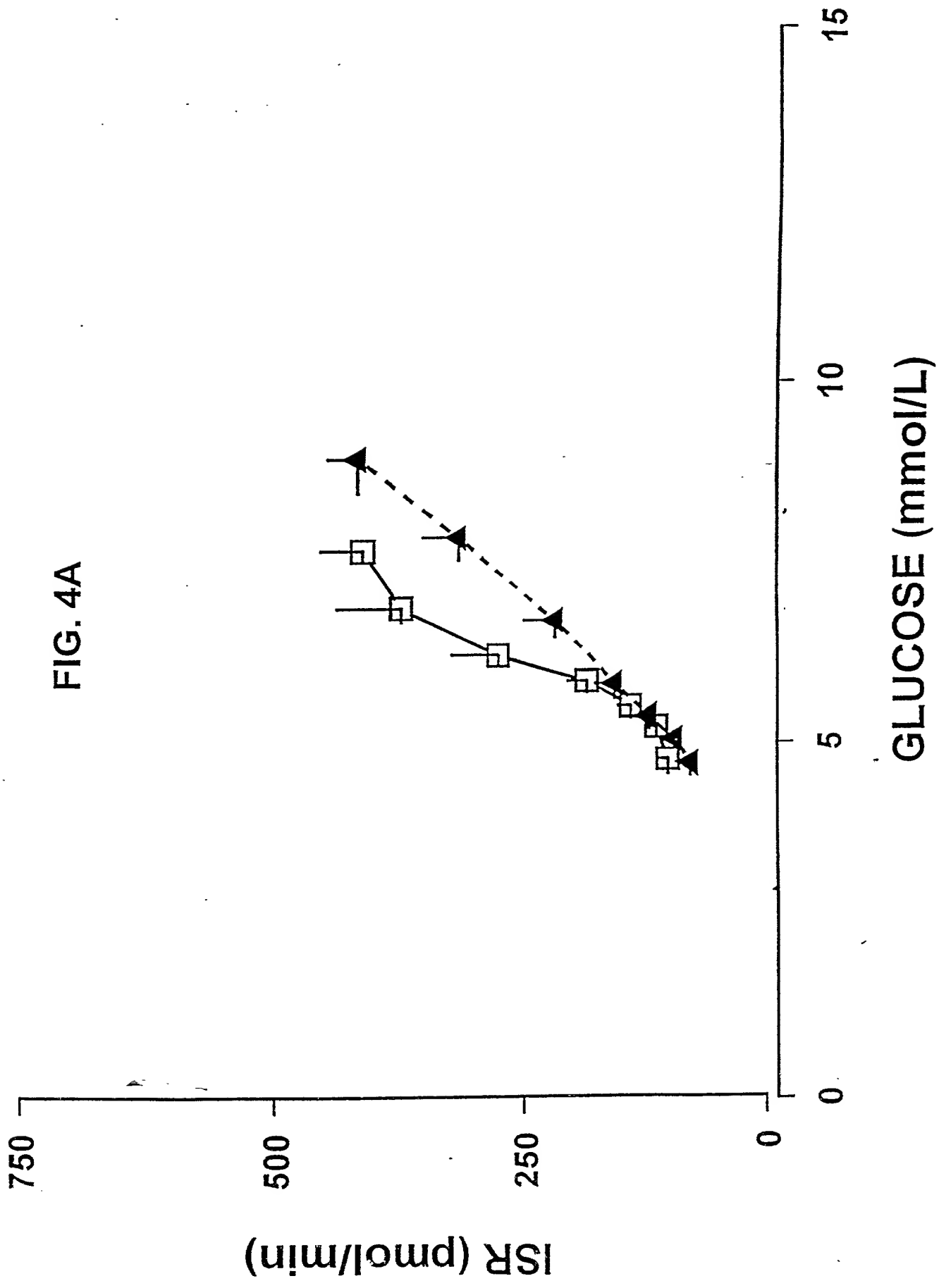


FIG. 3





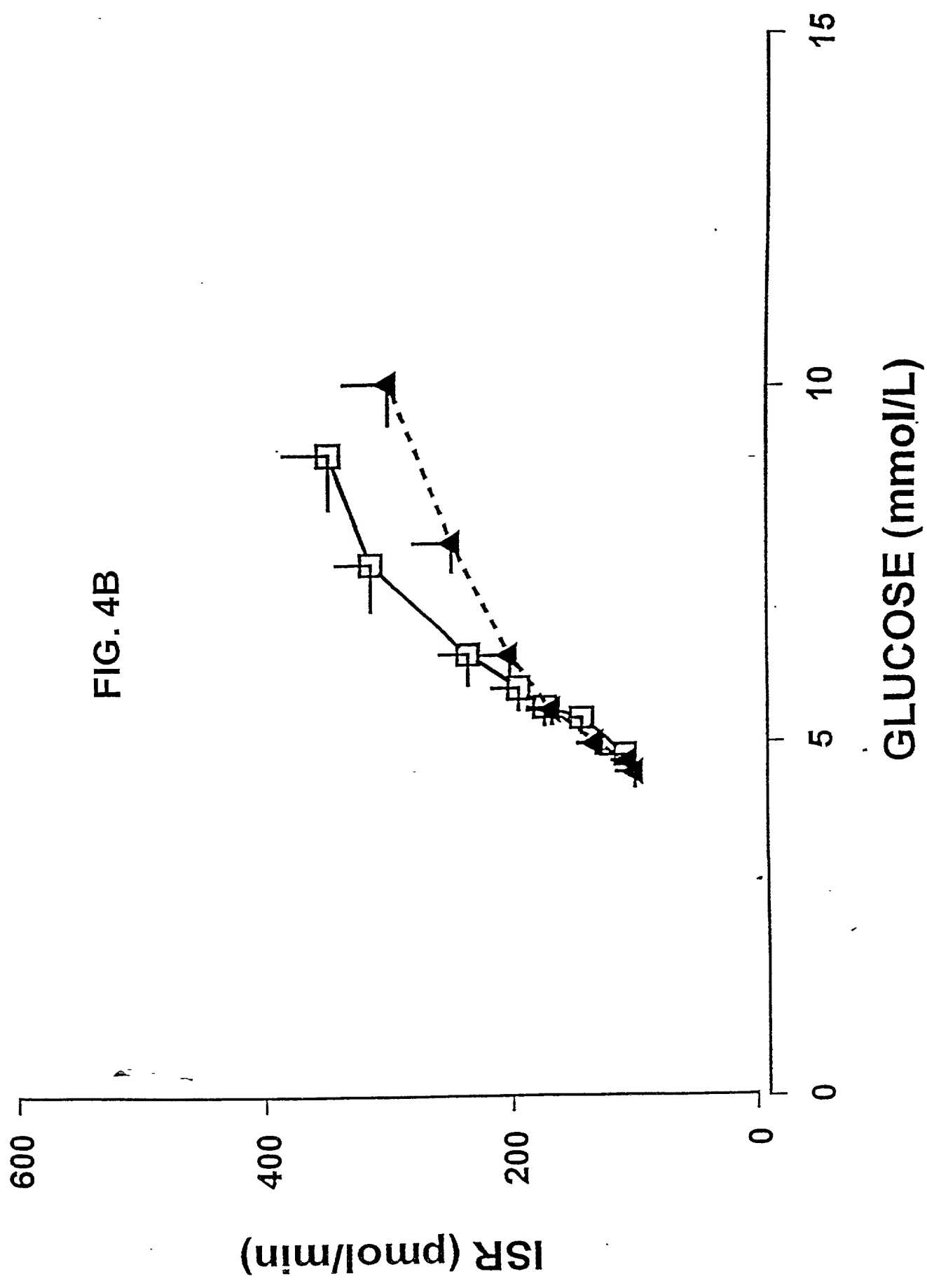
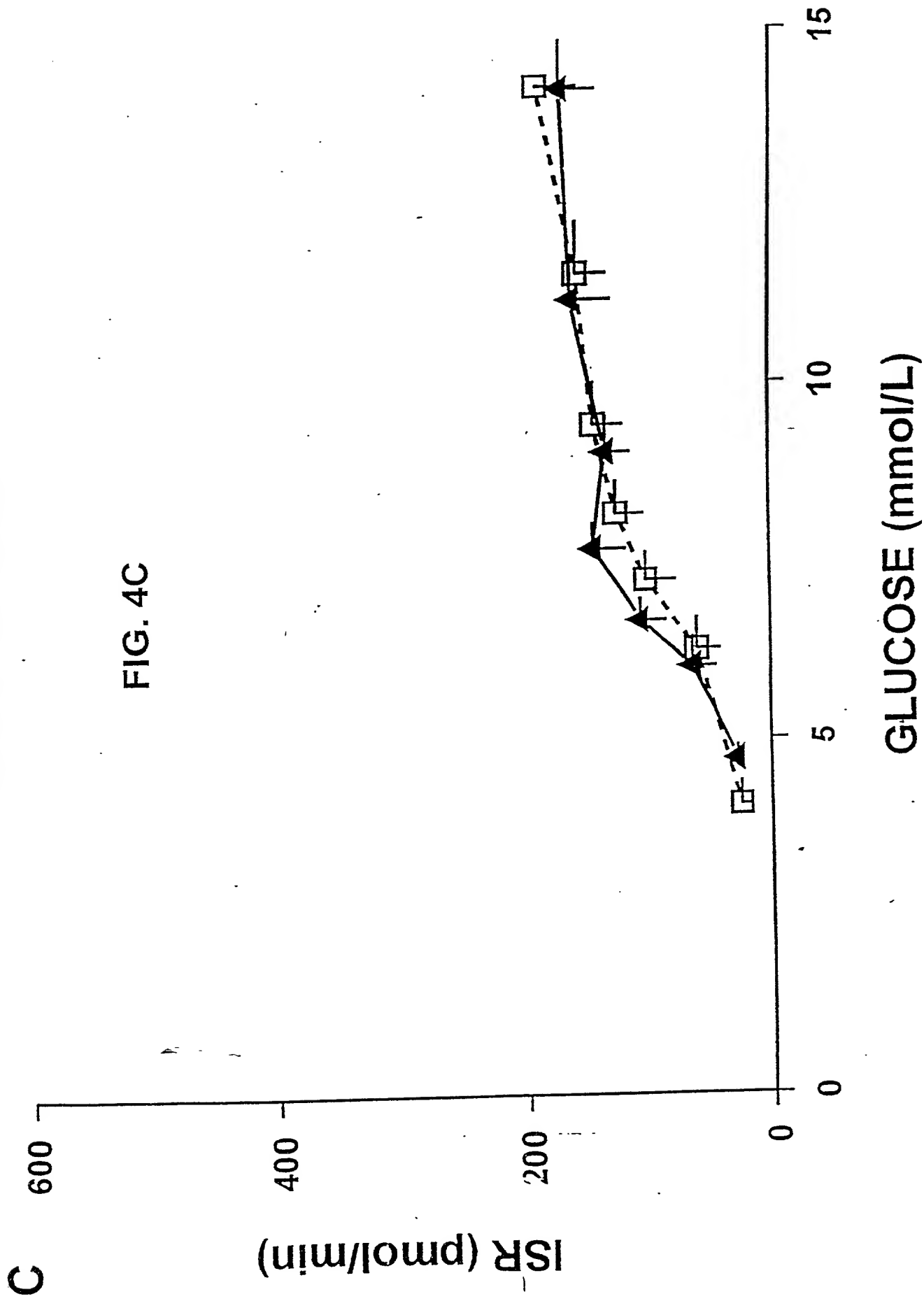
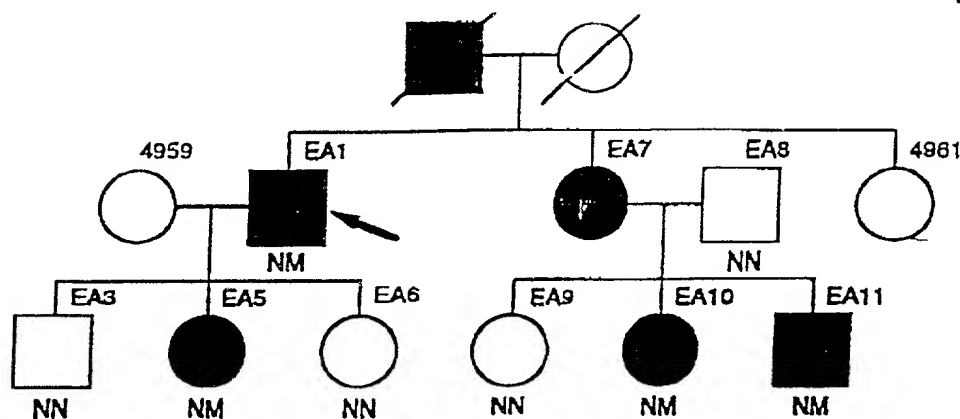


FIG. 4C



A. Edinburgh Pedigree

FIG. 5A



Frameshift mutation, insertion of C in codon 289, Exon 4; CCC→CCCC

B. H Pedigree

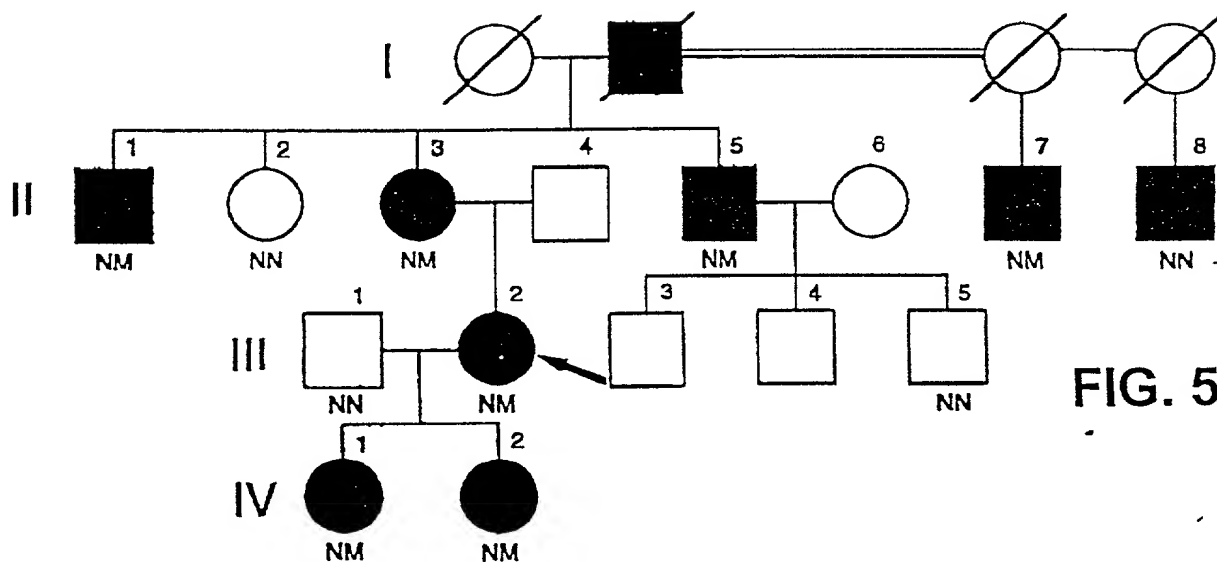
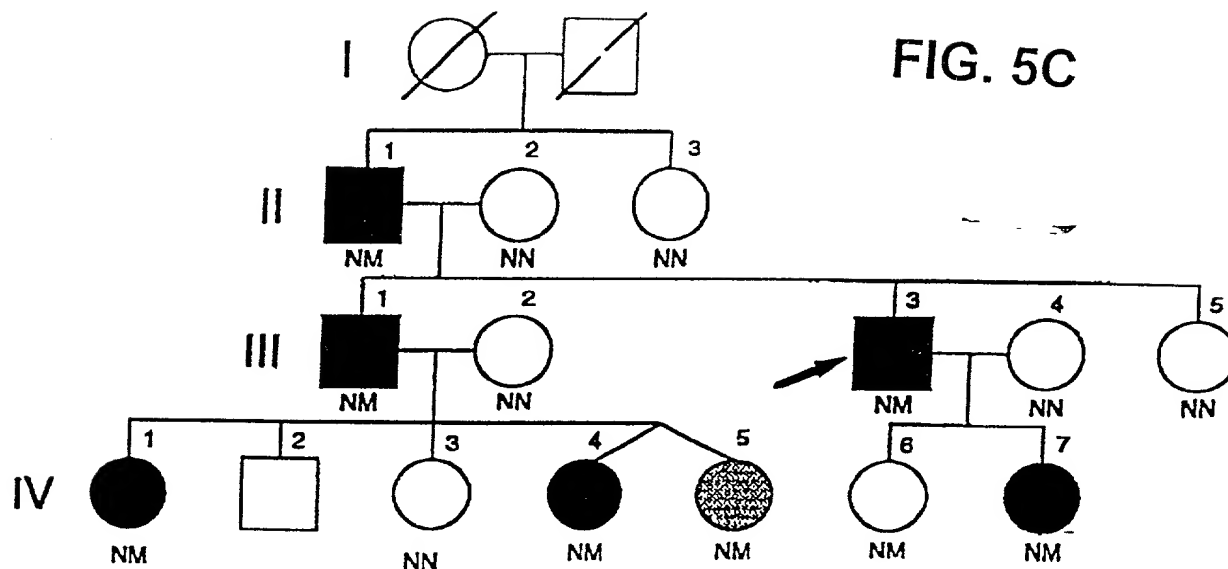


FIG. 5B

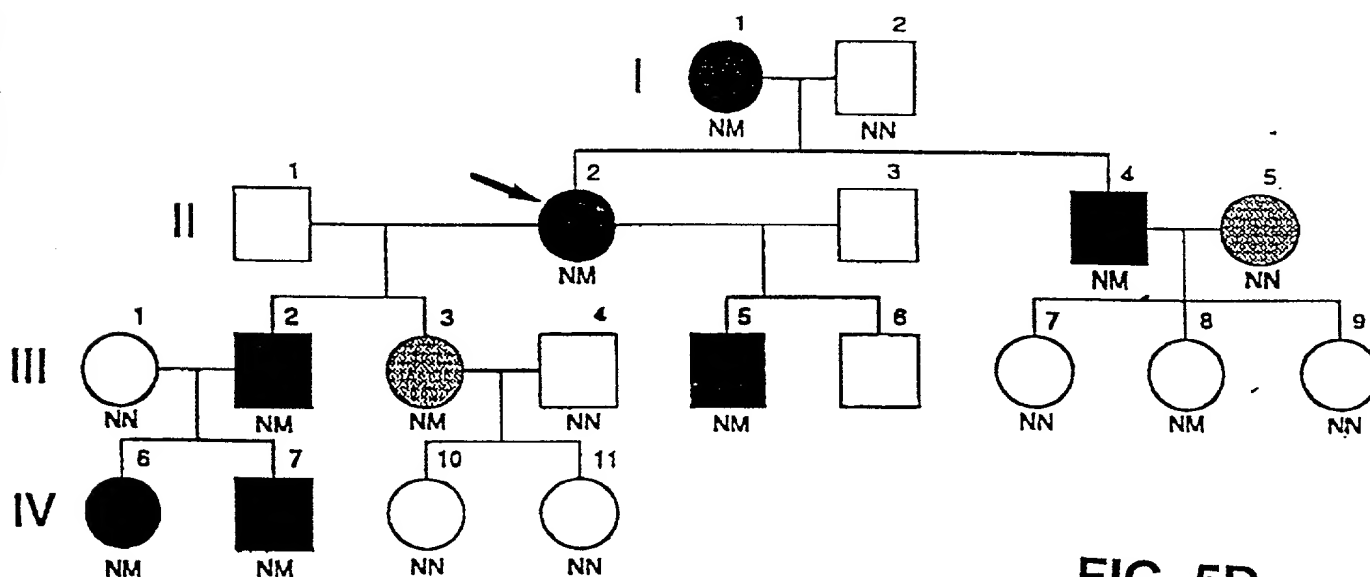
Missence mutation, codon 131, Exon 2; CGG (Arg)→CAG (Gln)

C. P Pedigree



Splicing mutation - splice acceptor site of Intron 5; AG→GG

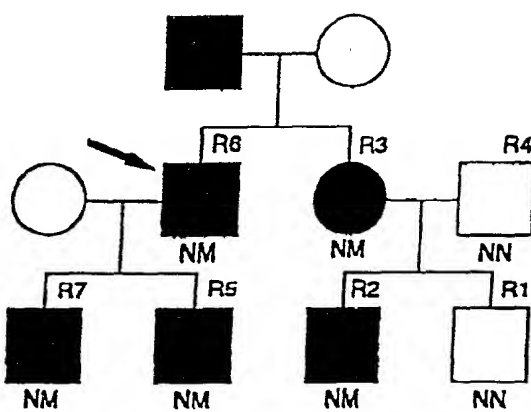
D. GK Pedigree



Splicing mutation - splice donor site of Intron 9; GT→AT

G. R Pedigree

FIG. 5G



Frameshift mutation - CT deletion codon 379, Exon 6; CCT→C

FIG. 5G

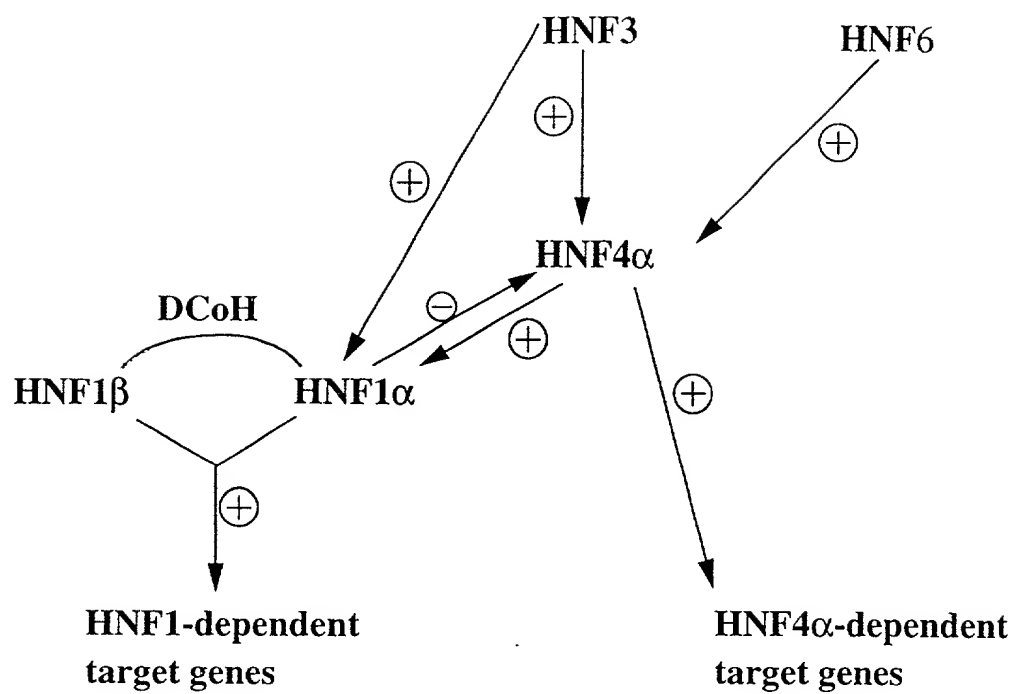


FIG. 6

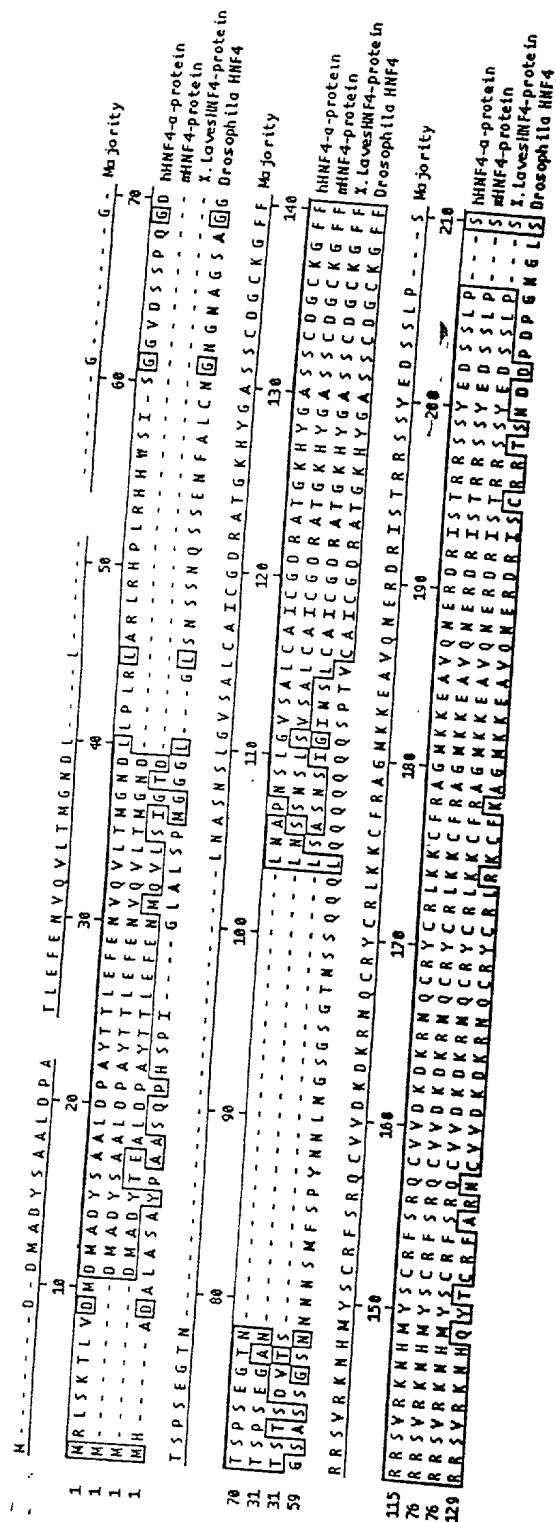


Fig. 7A

228	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
230	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
232	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
234	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
236	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
238	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
240	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
242	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
244	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
246	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
248	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-</																																																								

Fig. 7B

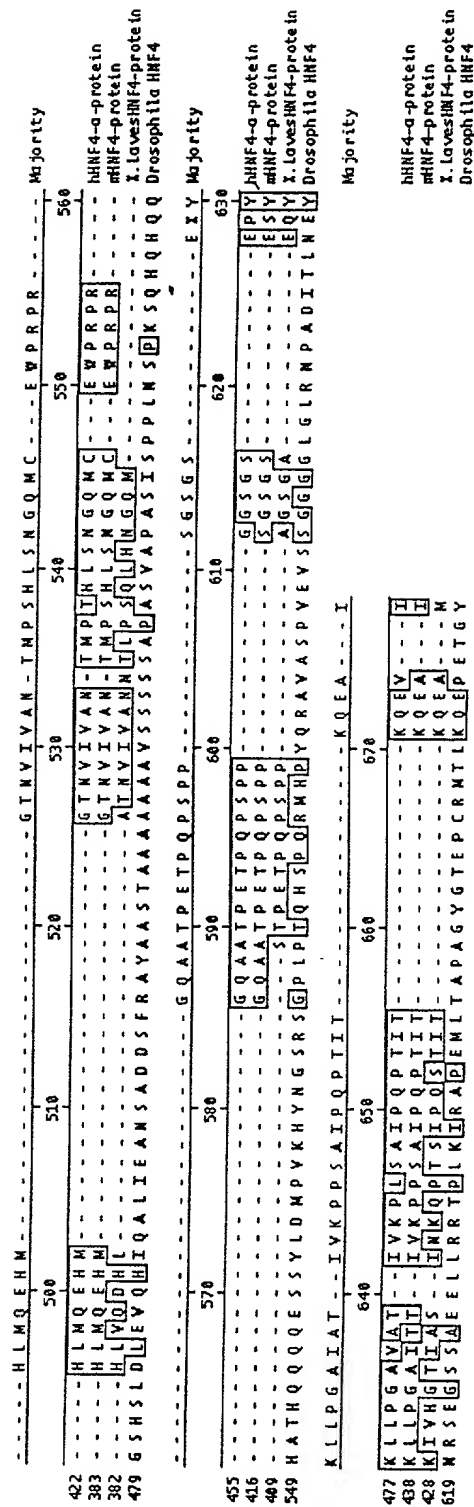


Fig. 7C

FIG. 8A. Partial Sequence of Human HNF4 Gene
(Exon 1 SEQ ID NO:34)

GCAGAGAGGG CACTGGGAGG AGGCAGTGGG AGGGCGGAGG
GCGGGGGCCT TCGGGGTGGG CGCCCAGGGT AGGGCAGGTG
GCCGCGGCGT GGAGGCAGGG AGAATGCGAC TCTCGAAAAC
CCTCGTCGAC ATGGACATGG CCGACTACAG TGCTGCACTG
GACCCAGCCT ACACCACCCT GGAATTTGAG AATGTGCAGG

TGTTGACGAT GGGCAATGGT AGGTGGGGGC AGATGTGCCC
AGGTGTGCCA GTGGGGGGCAG GTGTGCCTGG GTCCAGGAGC
AGATCTTTGG CACTCAACTT TGGGGTGGGA GGAGAATGAT
ACAAAATGGT AGGTTGGTCC TACAGGCCAG CACAGGTGTT
GCCAAGTGAA GCCCATGTGC CCAGGCACAG TGATCACAGG

CATTCTGGGT GAAGGGAGGC CTGCAAGGGC CAATTTCCAG
CAAAAGTCGA TCCCGGCTAT TCCTCCCAGG CCCTTCCAGT
CCTCACTGCC TCACAGTGGC TCTGCTTGGC GCTTGGCACA
GTGACATGAT GGTGAGCTCC CCCTTGGTGC CCAGCTCCAG
CGATTCAGCC CAGCACGGCC CCTTCGTGAA CCCCTTGGGC

CTAGGTTCAG AGAGACGGCA AGGGATGTTG TATCCCTGGA
GATGGTGGTT GGAGACATAA CCGCATTTCT C

FIG. 8B. Partial Sequence of Human HNF4 gene
(Exon 1b SEQ ID NO:36)

TGGATGTTTG TACATGTGTG CTGTGTGTGC GGGTCATAGA
GCACATGTGT TTGTGCATGC GGACCTGTTG GAGTGCCCTG
TTCTTCCTGC ATCTTTATCC TGTATGGGCG TTTTGTCGTG
TGCCCATATT TGTACCTGCT GTGTATATAT GCAGTTCCCT
GTGCTGCGGG CGGGGGTCAG CGGTCTCTGG TGTGCACGAC

TGCACAGACC CAAATGCAGG ACTCTGTTGT TGCCACTCAC
CAAGTGAGAT TCATATCAGC AACATGTCCG TTTGTCTCTG
AGCAGATTTG TTGCCGCTGC GTCTCGCCAG ATTGAGGCAT
CCCCTCCGAC ATCACTGGAG CATATCTGGA GGGGTGGACA
GTTCTCCACA GGGAGGTAGG GGAAAAGAGG AGGCCCGGAA

ACCCCTCCTG GAGGGAAGAG CCCCATCGGT CCCAGGCCAG
CCTCAGAGGA GAGGGGGCAG GCAGCTGGCT GAGGTCAGCC
TYGCCACCCTG CTTCTTCTG TGTCTTGGAG CCACTCAGCC
AGTATGAGGC TGCAGCTCCA GCTGAGGTCT GGAATCTTGT
GGTCAGCTCA GCTAGGGTGA GGAGGCAGCT GCTGGGCACT

GCTTGTTGTC AGCTCAGCAG GTGCTCACCT GCCCCTGCCG
TCCAGTCACG TGTGACCTTG GGCATGTCAC CTCCCCTATC
CTGGCTTCTG TATCTTCTAC AAAACAGGCT TCATTCCCCC
AGGCCTGCTG GCTGGACGGC TTTTAGGCCT GTCTGAGGAC
CACGCCAGGA GCGCAAGGCA AAAACACACC AGAGAT

FIG. 8C. Partial Sequence of Human HNF4 Gene
(Exon 2 SEQ ID NO:38)

CCCCTTGCGA GTTAGGAGGC CGGCTCCAC CCCAGAAGGT
GGCCAGGTTT TCATGCCTTC CTAGAGAAAG CTGGGGCTGG
TGGCCTCCAC CACAGGGAGA CGCAGACCCT CAGAAACAAG
TCTGTGAAGT CACAACCAGC CCCAGTTTAC AGATGTGAAA
CTGAAGCTCC AAAAAGTCAG GAGGTCACTG AGTGGGGAGG

TGATGGAGTG GAACAGCCCC CAGATCTGGC TGAGGCCGAA
GCCCTGGAGA GATCCCCGCA AGGCTCCCTT AGATGCCTGA
CATTCTGTTC TTCCTGAAGC CTCACTCCCT TCTCTCCTGG -
CGCAGACACG TCCCCATCAG AAGGCACCAA CCTCAACGCG
CCCAACAGCC TGGGTGTCAG CGCCCTGTGT GCCATCTGCG

GGGACCGGGC CACGGGCAAA CACTACGGTG CCTCGAGCTG
TGACGGCTGC AAGGGCTTCT TCCGGAGGAG CGTGCGGAAG
AACCACATGT ACTCCTGCAG GTGAGGAGCC TCAATTTCTT
CAGCTGGGAA ATGGGCACAC TTGGGCTCAT GGCCCCAAGG
TCTGTCTTCT CCCTGAGTGG GTAGGTCCCA GAGACAGCTG

CCCTTCAGGG CCTTCAAGGC TCCTTCTGGTT TTGT

FIG. 8C. Partial Sequence of Human HNF4 Gene

FIG. 8D. Partial Sequence of Human HNF4 Gene
(Exon 3, SEQ ID NO:40)

AGAGAGTTCA TAGCACCTTT CCAGCTCCTG GTGGGTTCAA
GAGAGAACTC CCGGGATGAA GAGATGAGAG CACTGAGGTT
GGGGGGTCAA CTGGATAGCC AGGGCCCTAG TTCTGTCCTA
AGAGGAGGAA GTTGTGTCTT CTCCATCCAA CCATCCAAAAG
ACCTCCCCAG ATTTAGCCGG CAGTGCGTGG TGGACAAAGA

CAAGAGGAAC CAGTGCCGCT ACTGCAGGCT CAAGAAATGC
TTCCGGGCTG GCATGAAGAA GGAAGGTGAG CCTCGGCCCT
CCCCGCCCCA CCACCACTGC ACCACCTGCA CCCACAGCTC
CCCGACAGTC ATTTACAACT GTAGCCACAC TTTATGACTC
AGTGGCAGGC CCCAGGGTGA CTGGCTAATG GCTGAGAAGA

GGGAGGGCCT GGAAATCTGA CCATAGGGAG CGGCTGGGCT
TGGTCTTGAG AAAGATTC

FIG. 8E. Partial Sequence of Human HNF4 Gene
(Exon 4 SEQ ID NO:42)

tcccactcct catcagtcac agacaccccc accccctact
ccatccctgt tctccctcct cacctctctg tgcctcctca
cagCCGTCCA GAATGAGCGG GACCGGATCA GCACTEGAAG
GTCAAGCTAT GAGGACAGCA GCCTGCCCTC CATCAATGCG
CTCCTGCAGG CGGAGGTCCT GTCCCGACAG GTACCGGGGT

GATCCTGCCA CCCACCCAGG GGATCCCCCA CACTACAGAG
GAGCTCACCT CCTCCACCTC CATTCTCCCC AGCCAGGCCC
TGGAGCAGCT GACGGGAGGG GCCTCAGATA TTACAGAAGG
GACACTGAGT GCGGTTTCAC ATGGCCCAGT TTGCAGCAAG
GGCAGGAATC GAACCTGGCG CCCTGGGGCA CTTTCTAATT

CATCCTACTG CCTGCATCCC ACAGGCCAAG CAGAGTCTTC
ACCTTCACTG AGGGCCTGCG ATCAGCTCAG CTCCGAGAGA
ACAGAGCAGT GGCTCAGTGG AGAGAGGTGG CAAAGTGGGG
CCCAGCCCTT CCCTTGCTGA GTGACCTTGG GCAAGTCACA
GCACCTCTCT GAGCCATGGT TGCCTCATTG TCAGAAAAGG

ATGATGATTT TTTGCCTGC TTCTCCTCTA AGGCTGACAG
ACTCCTTGGG GCTCTAAAGC TG

FIG. 8F. Partial Sequence of Human HNF4 Gene
(Exon 5, SEQ ID NO:44)

TTCTCCTCA TCCCTGCCTC CTCCTCCCT CCGTTTTTAC
CCTGAGCTTC CTTCAGAGCT GGAGGGCACC CACTATCCAG
CCCCCTCCCC ACATCTGATT CCAGGGAGGG GGCTCTGTGC
AGGGGACAGA GAATGCGGGA GGGCCCGGAC ATCTCCAGCA
TTTTCTTCCC TGTATCTCTC GAAGATCACC TCCCCCGTCT

CCGGGATCAA CGGCGACATT CGGGCGAAGA AGATTGCCAG
CATCGCAGAT GTGTGTGAGT CCATGAAGGA GCAGCTGCTG
GTTCTCGTTG AGTGGGCCAA GTACATCCCA GCTTTCTGCG
AGCTCCCCCT GGACGACCAG GTGAGGATGG GCGTGGATGG
TGGGCAGTAG TGGGCAGTGG GCGGGGCAGC CAGGGGGCTG

CTGGCCCACC TGGGATATAG CCGTGGACTG GCTTGATTTT
ATTTTATTTA ACAAATATG TAGTGACAC ACGTGTCTGA
AACTTTAAAT CACCTTACAA ATATTAAGTC AGTTAGCTCC
TCCAACAACCT CTATGAGGTA GGTACTAAGG TACTATTATT
ACTGCCATCT CATAGGTGAG AGATTGGGGC ACAGAGAGGT

TAAGTAACCT GCTCAAGGTC ACATAGCTAC TATCCAGCAT
AGCTGGG

FIG. 8F-3074260

FIG. 8G. Partial Sequence of Human HNF4 Gene
(Exon 6, SEQ ID NO:46)

ATTTTACAA AGCACCTTC ATAATTCTCC ATAGCTGGTC
CATGGGTGGG AATTTGGGAC CCACAGTTTT GGAAC~~T~~TTT
GGGATCATAG ACCTTTTTGA GAATCTCAAA AAAGAAAAAA
AAGCACACAG AATGTTGCTT ACAGTTTCAT CAGGCACACA
GAAGAGGCC AGCACGAAGC AGTTTCTTGC CCAAGGACAC

AGCAGTTCAA GGACAGAGTC AGCGCGAGGT CTCTCAGCTC
TGAGCACATG TTCTTTCCCC TTCCAGGTTT CTAGTTTTAT
GGGTAGTAGT TTTATGATGC CCATTTCAACA GTTCAGGCAG
GTAGAGGCAG AGGGGAGCAT TAAGCTGACT TGCCCAGCGT
CACTGAGTTG GCTACGGGCA GCCTTCCCAA GGGTACAGAT

GGCAAACACT GTTCCTTATC TCTTTCAGGT GGCCCTGCTC
AGAGCCCATG CTGGCGAGCA CCTGCTGCTC GGAGCCACCA
AGAGATCCAT GGTGTTCAAG GACGTGCTGC TCCTAGGTGA
GGCGGCTGCC TGCCCTGGCC AGGGCTCCAG GGAGGGTATG
CCTAGCATGG CACTCACCCA GGCAAGGAGA TTCACATGGT

GGCATGCAAG GGTGAGGGAG ACTAGTCAGG AGTGGCCCTG
TCCTCAGGCT TGCATTGGAG GGCTCCAGGA CTCAGTTTTC
AACTGGGTAC CCCACTCAGA TGCAAGGAAA TGTGGATGCA
AGTCACCAAA TTCCCAGCAT TGAAGTCAGA GCACGATCAG
GGTTATCCCT GGAATTACCT GTGCATCCTT TTTTCTTTTG

ACAGAGTCTT GCTCTGTCAC TCAGGCTGGA GTGCAATGAT
GTGA

FIG. 8H. Partial Sequence of Human HNF4 Gene
(exon 7, SEQ ID NO:48)

GCAACACTAG TATTTTAATA TAACAATGCT ATGAGGGAGC
TCGATTATTT ATCCTCATCT TATAGATAAG AAAACTGAGG
CACAGAGAGG TTAAGTAACT TATCCAATA TAACCAGCTA
TCAGGGGCAG AGCCATTAA GCAGGGCAGT GCAGTTCCAG
AATCTGGTCC TTAAACCTTG ATGCTTTGGT GCCTATCAGG

TGACCTTTGA ATGTCATCGA TCTTGTGAGT CATGTTGGTA
AATGGAGCTT GGGTCATGTG AAAGAGGTCC TAGAAAGCCA
AGTTCCAAGC TCAGCCGGAT GACTCAAGGC AGCTTATCTT
CTGAATCTGG GCCTCAGCTT CCTTACCTGT GAAATGGGAG
TCACCATCCC TGCAGGTCCT CCTCCACAG GCACCAGCTA

TCTTGCCAAC TTAAAAGCCA AACTAGAGG AGAGGGGTCA
ACCAAAGTG ACTTCCCATC CTCCCTCCCT CCCAACCCTT
CCAGGCAATG ACTACATTGT CCCTCGGCAC TGCCCGGAGC
TGGCGGAGAT GAGCCGGGTG TCCATACGCA TCCTTGACGA
GCTGGTGCTG CCCTTCAGG AGCTGCAGAT CGATGACAAT

GAGTATGCCT ACCTCAAAGC CATCATCTTC TTTGACCCAG
GTACAGTGCA CACCTCCTAA GCCATCCCTG ACTCTCTCTC
CAGAACGCTC TGCCAGACTT CTCCTATTGG GTTCTGTACA
CTGAGTTCAC AGCCTCATCT CATGTAAACG ACAGCCAGGA
GAGGCCGTTT TCATTAAACA GATGAGGCAA GTCAAGATT

GAAGAGACAA TATGGCCGGG CGCAGTGGCT CACACCTGTA
ATCCCATCAC TTTGGGAGGC TGAGGCGGGC GGATCACCTG
AGGTCAGGGG TCAAGATGAG CCTGGCTAAC ATGGAGAAAC
CCCATCTCTA CTAAAA

FIG. 8I. Partial Sequence of Human HNF4 Gene
(Exon 8 SEQ ID NO:50)

GTGGCTCTGC CAACAACTGG CTGTGCGACC CAGGACAAGT
CCTATCTTTG CACTGTGTCT GGGTTTCCCC GTGTGTAAGA
TGAGGCGGTT GCTAGGTGCT TATTGGATGC ATTCCTCAAG
TCCCGCCCTC CATCTCCTAT TCCCCTCTCT TCTGGTTTAG
TGCTTTAGGA AATGTGGCAG AAATCTTTTT CTGCCTGTGT

CTAGGAAATC ATAATTCATG CTGGCGTACC CTGGTTGTTG
AGGTCCCTGA ATCCTTGTGC CCACACTGCT GAAGACTCCT
TGTGTGACAC AAGTCAGGGG ACATCTGGGT CTTGACTCCC
CAGATGCTCC AGGTGGACCC TGCTGCCCTC CCTTGCCAC
CCTCTTCCAT TGTAGATGCC AAGGGGCTGA GCGATCCAGG

GAAGATCAAG CGGCTGCGTT CCCAGGTGCA GGTGAGCTTG
GAGGACTACA TCAACGACCG CCAGTATGAC TCGCGTGGCC
GCTTTGGAGA GCTGCTGCTG CTGCTGCCCA CCTTGACAGAG
CATCACGTGG CAGATGATCG AGCAGATCCA GTTCATCAAG
CTCTTCGGCA TGGCCAAGAT TGACAACCTG TTGGAGGAGA

TGCTGCTGGG AGGTCCGTGC CAAGCCCAGG AGGGGCGGGG
TTGGATTGGG GACTCCCCAG GAGACAGGCC TCACACAGTG
AGCTCACCCC TCAGCTCCTT GGCTTCCCCA CTGTGCCGCT
TTGGGCAAGT TGCTTAACCT GTCTGTGCCT CAGTTTCCTC
ACCAGAAAAA TGGGAACAAG GCAATGGTCT ATTTGTTCA

GCACCGAGAA CCTAGCACGT GCCAGTCACT GTTCTAAGTG
CTGGCAATTC AGCAAAGAAC AAGATCTTTG CCCTCGGGGA
GGCTGTGTGT GTGTGATAT GTATGGATGC GTGGATATCT
GTGTATATGC CCGTATGTGC GTGCATGTGT ATATAAAGCC
TCACATTTTA TGATTTTGA

FIG. 8J. Partial Sequence of Human HNF4 Gene
(exon 9, SEQ ID NO:52)

GGGACACATA GATGCTATAA GTAGGTCAGT TGGCTGCAGC
AGAGATGTGG GGGATGAGGC TGAAAGGTGA GGCGGGAGCA
AATGGTTGAA GGACTTGCAC TCCAAGGAGC TTTGAGAGCC
ATTGATTACA TCCATTATGT TACTATGTGA CCAATACATT
ACTCATTAGA ACATTTACGT GATCTCAGAG CTTCCTTATA

TGCACCTTGT TCCTTTCAAC TCACTTTTGT TCTCTTGGTT
TTTTGGGGTC CTCTTAACAC CCTCATGAAG TCTATAGATG
GGAATGGTAC ACCCTAGTTT ACTAACCCAG GAATAGGTAC
CCAACAGGCA CTGCCAATAT TGGATGGGCT GGTTGATTGG
CCACGCCTGA GGAAGATGGC GTCCCAAGGC CTGAGGTCTG

CATCCCAGAC TCTCCATCCT GATCGACCTT CTCTACCTGC
AGGGTCCCCC AGCGATGCAC CCCATGCCCA CCACCCCCTG
CACCTCACC TGATGCAGGA ACATATGGGA ACCAACGTCA
TCGTTGCCAA CACAATGCCC ACTCACCTCA GCAACGGACA
GATGTGTGAG TGGCCCCGAC CCAGGGGACA GGCAGGTGGG

CAAACCTCTGG GATTTTACCT TGCAAAGGGT GAGGATGGGG
CTTAAGACAG GAGGCAGGAG AAAGTGGAGT CTAGAAGGTA
GAACCAGGAT GCAACAGTTT TCTGGGTTCC AGGGTAGGGA
ATAAAGGGCA AGATTGTCCA TTTGTTGAGG CTGTTTATTC
AGTAAGGTGA CTGACAGCCT TTAAGTAATG AAGCCATTGT

TGGGATGAGG CAATCCACTG GATGAGGTAA CCCATTGGGT
GAAGATGTCT TGGGTGAGAA TTCCATTAGT TGACATTGTC
CATTAAAGTAA AAGTGGTCAT TGAAGTAAGG CTGCACAGTT
GGGTAAGGCT ATCCATTAGA CATTAGATGA GACTACCCAT
TGGGTCAGGA TGTCTGCTGG GCTA

FIG. 8K. Partial Sequence of Human HNF4 Gene
(Exon 10 SEQ ID NO:54)

TTTGGGAGAA GCAGTCCAAG TCTGCATATC AAATAAATGA
TGGAGGAGAT GGGTGGTAGG ACCTTCCAGA CCTCATAAAA
CTTAGGCTTT ATGATCTGGG ACTCACAGAA GGTGAGCAA
TAAAAGACCT TAGGGATTAT CTGGCTTAAT TAATTCTCTC
ATTTTATAGA GGAAGAAATT AAGTCAAGGT GGGGCAGGGT

GGGAGGGGAG AACTTTCCCG GGGCTCTTCA TTTACTCCCA
CAAAGGCTGG AATTTTGAGC AGCCCCTGTC TGTCTGTTTG
TCCTTCCAGC CACCCCTGAG ACCCCACAGC CCTCACCGCG
AGGTGGCTCA GGGTCTGAGC CCTATAAGCT CCTGCCGGGA
GCCGTCGCCA CAATCGTCAA GCCCCTCTCT GCCATCCCCC

AGCCGACCAT CACCAAGCAG GAAGTTATCT AGCAAGCCGC
TGGGGCTTGG GGGCTCCACT GGCTCCCCC AGCCCCCTAA
GAGAGCACCT GGTGATCACG TGGTCACGGC AAAGGAAGAC
GTGATGCCAG GACCAGTCCC AGAGCAGGAA TGGGAAGGAT
GAAGGGCCCC AGAACATGGC CTAAGGCACA TCCCACTGCA

CCCTGACGCC CTGCTCTGAT AACAAGACTT TGACTTGGGG
AGACCCTCTA CTGCCTTGGA CAACTTTCTC ATGTTGAAGC
CACTGCCTTC ACCTTCACCT TCATCCATGT CCAACCCCCG
ACTTCATCCC AAAGGACAGC CGCCTGGAGA TGACTTGAGC
CTTACTTAAA CCCAGCTCCC TTCTTCCCTA GCCTGGTGCT

TCTCCTCTCC TAGCCCCGGT CATGGTGTCC AGACAGAGCC
CTGTGAGGCT GGGTCCAATT GTGGCACTTG GGGCACCTTG
CTCCTCCTTC TGCTGCTGCC CCCACCTCTG CTGCCTCCCT
CTGCTGTCAC CTTGCTCAGC CATCCCGTCT TCTCCAACAC
CACCTCTACA GAGGCCAAGG AGGCCTTGGA AACGATTCCC

CCAGTCATTC TGGGAACATG TTGTAAGCAC TGACTGGGAC
CAGGCACCAG GCAGGGTCTA GAAGGCTGTG GTGAGGGAAG
ACGCCTTTCT CCTCCAACCC AAC

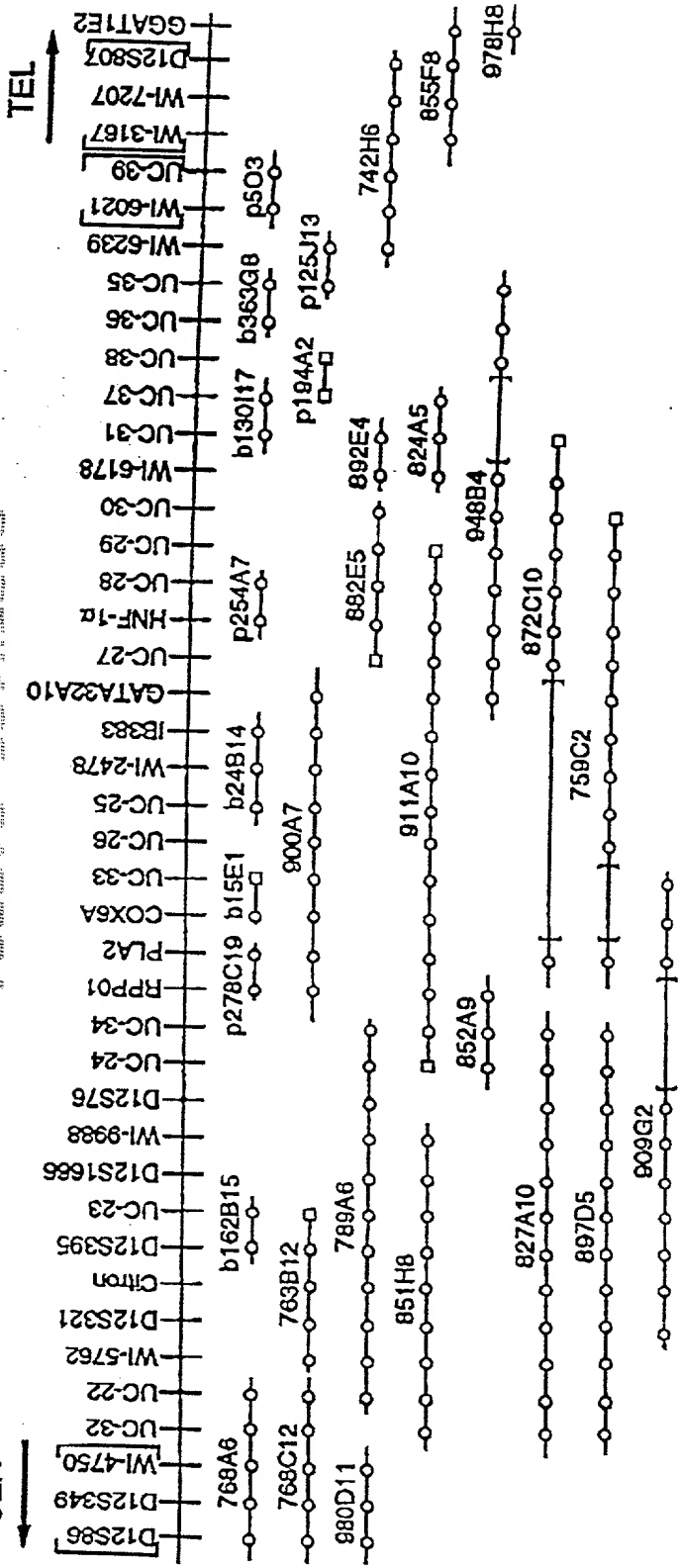


Fig. 9

Fig. 10A

Normal Allele

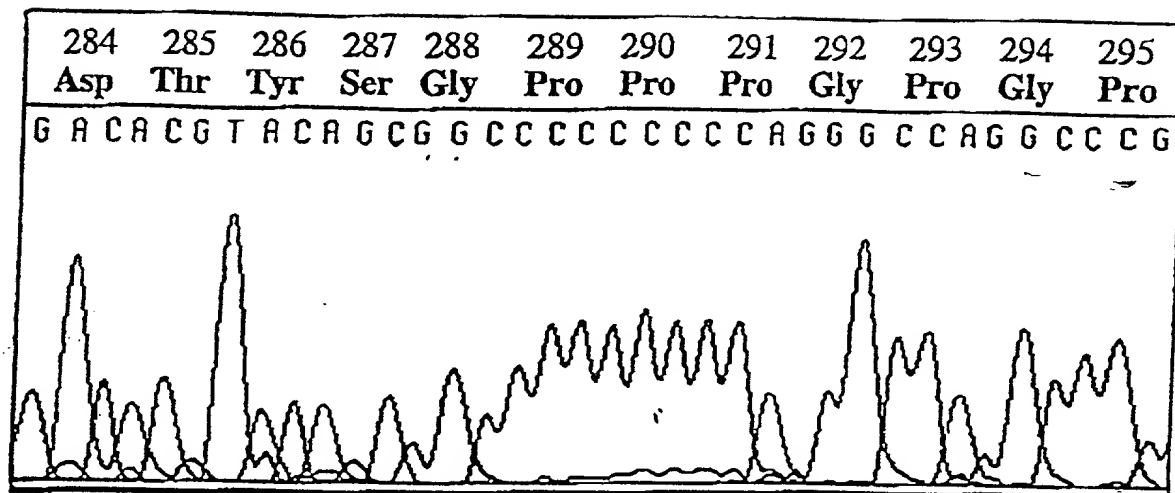


Fig. 10B

. Mutant Allele

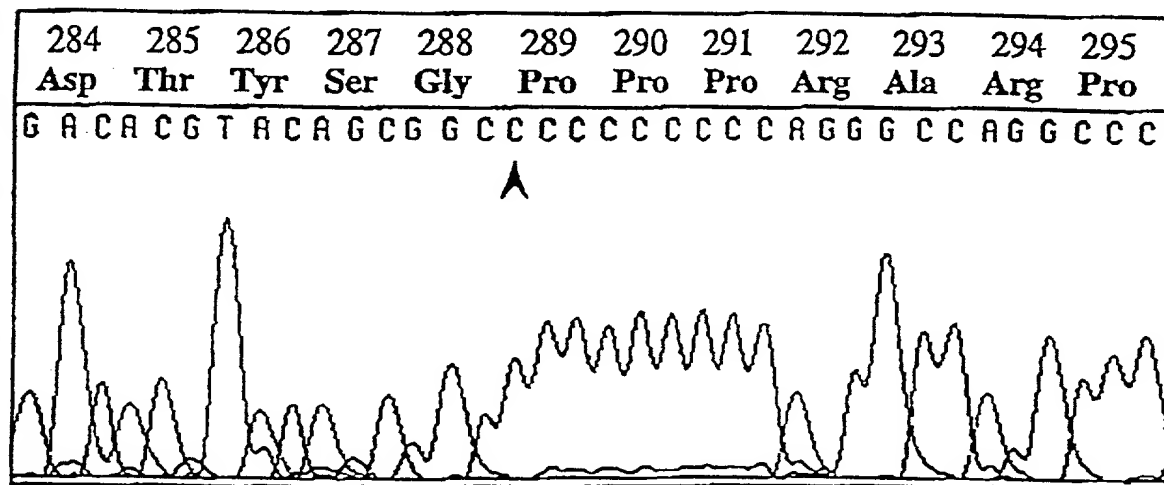


FIG. 11. Translation of human HNF1a sequence (cDNA=SEQ ID NO:1 and protein=SEQ ID NO:2)

1	10
Met Val Ser Lys Leu Ser Gln Leu Gln Thr Glu Leu Leu Ala Ala Leu Leu Glu Ser Gly Leu Ser Lys Glu	
ATG GTT TCT AAA CTG ACC CAG CTG CAG ACG GAG CTC CTG GCG GCC CTG CAG TCA GGG CTG ACC AAA GAG	
30	40
Ala Leu Ile Gln Ala Leu Gly Glu Pro Tyr Leu Leu Ala Gly Glu Gly Pro Leu Asp Lys Gly Glu Ser Cys Gly Gly Arg	
GCA CTG ATC CAG GCA CTG GGT CAG CCG GCG CCC TAC CTC CTG GCT GGA GAA GGC CCC CTG GAC AAG GGG GAG TTC TCC GGC GGC GGT CGA	
60	70
Gly Glu Leu Ala Glu Leu Pro Asn Gly Leu Gly Glu Thr Arg Gly Ser Glu Asp Glu Thr Asp Asp Gly Glu Asp Phe Thr Pro Pro	
GAG CTG GCT CAG CTG CCC AAT GGG CTG GGG GAG ACT CCG GGC TTC GAG GAC CAG ACG GAC GAC GAT GGG GAA GAC TTC ACG CCA CCC	
90	100
Exon 1/ 110 Exon 2	
Ile Leu Lys Glu Leu Glu Asn Leu Ser Pro Glu Glu Ala Ala His Gln Lys Ala Val Val Glu Thr Leu Leu Gln Glu Asp Pro Trp Arg	
ATC CTC AAA GAG CTG GAG AAC CTC ACC CCT CAG GAG GAG GCG GCC CAC CAG AAA GCC GTG GTG GAG ACC CTT CTG CAG GAG GAC CCG TGG CGT	
120	130 Gln (Hinek- missense)
	140

Val Ala Lys Met Val Lys Ser Tyr Leu Gln Gln His Asn Ile Pro Gln Arg Glu Val Val Asp Thr Thr Gly Leu Asn Gln Ser His Leu
GTG GCG AAG ATG GTC AAG TCC TAC CTG CAG CAG CAC AAC ATC CCA CAG CCG GAG GTG GTC GAT ACC ACT GGC CTC AAC CAG TCC CAC CTG

A

150

160

170

Exon 2

Ser Gln His Leu Asn Lys Gly Thr Pro Met Lys Thr Gln Lys Arg Ala Ala Leu Tyr Thr Trp Tyr Val Arg Lys Gln Arg Glu Val Ala
TCC CAA CAC CTC AAC AAG GGC ACT CCC ATG AAG ACG CAG AAG CCG GGC CTC TAC ACC TGG TAC GTC CCG AAG CAG CGA CAG GTG GCG

Exon 3

180

190

200

Gln Gln Phe Thr His Ala Gly Gln Gly Gly Leu Ile Glu Glu Pro Thr Gly Asp Glu Leu Pro Thr Lys Lys Gly Arg Arg Asn Arg Phe
CAG CAG TTC ACC CAT GCA GCG CAG GGA GCG CTG ATT GAA GAG CCC ACA GGT GAT GAG CTA CCA ACC AAG AAG GCG CCG AAG AAC CGT TTC

210

220

230

Lys Trp Gly Pro Ala Ser Gln Gln Ile Leu Phe Gln Ala Tyr Glu Arg Gln Lys Asn Pro Ser Lys Glu Glu Arg Glu Thr Leu Val Glu
AAG TGG GGC CCA GCA TCC CAG CAG ATC CTG TTC CAG GGC TAT GAG AAG CAG AAG AAC CCT ACG AAG GAG CAG CGA GAG ACG CTA GTG GAG

Exon 3 | 240 Exon 4

250

260

Glu Qys Asn Arg Ala Glu Qys Ile Gln Arg Gly Val Ser Pro Ser Gln Ala Gln Gly Leu Gly Ser Asn Leu Val Thr Glu Val Arg Val
CAG TGC AAT AGG GCG GAA TGC ATC CAG AGA GCG GTG TCC CCA TCA CAG GCA CAG GCG CTG GGC TCC AAC CTC GTC ACG GAG GTG CGT GTC

270

280

290

Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu Glu Ala Phe Arg His Lys Leu Ala Met Asp Thr Tyr Ser Gly Pro Pro Gly Pro Gly

TAC AAC TGG TTT GCC AAC CCG CCG AAA GAA GAA GCC TTC CCG CAC AAG CTG GCC ATG GAC AGG TAC AGC GGG CCC CCC CCA GGG CCA GGC

CCCC (Donoghue - C insertion)

Exon 4 | 320 Exon 5
Pro Gly Pro Ala Leu Pro Ala His Ser Ser Pro Gly Leu Pro Pro Ala Leu Ser Pro Ser Lys Val His Gly Val Arg Gly Gln
CCG GGA CCT GCG CTG CCC GCT CAC AGC TTC CCT GGC CTG CCT CCA CCT GGC CTC TCC CCC AGT AAG GTC CAC G|GT GTG CCG TTT GGA CAG

330

340

Pro Ala Thr Ser Glu Thr Ala Glu Val Pro Ser Ser Ser Gly Gly Pro Leu Val Thr Val Ser Thr Pro Leu His Gln Val Ser Pro Thr
CCT GCG ACC AGT GAG ACT GCA GAA GTA CCC TCA AGC AGC GGC GGT CCC TTA GTG ACA GTG TCT ACA CCC CTC CAC CAA GTG TTC CCC ACG

(Pratt - mutation splice acceptor site Exon 6, AG --> GG)

360

Exon 5 | 370 Exon 6

Gly Leu Glu Pro Ser His Ser Leu Leu Ser Thr Glu Ala Lys Leu| Val Ser Ala Ala Gly Gly Pro Leu Pro Pro Val Ser Thr Leu Thr
GGC CTG GAG CCC AGC CAC AGC CTG CTG AGT ACA GAA GCC AAG CTG| GTC TCA GCA GCT GGG GGC CCC CTC CCC CCT GTC AGC ACC CTG ACA

C-- (Newton - CT deletion)

Ala Leu His Ser Leu Glu Gln Thr Ser Pro Gly Leu Asn Gln Gln Pro Gln Asn Leu Ile Met Ala Ser Leu Pro Gly Val Met Thr Ile
GCA CTG CAC AGC TTG GAG CAG ACA TTC CCA GGC CTG AAC CAG CAG CCC CAG AAC CTC ATC ATG GGC TCA CTT CCT GGG GTC ATG ACC ATC

420

430

Exon 6 | Exon 7 440

Gly Pro Gly Glu Pro Ala Ser Leu Gly Pro Thr Phe Thr Asn Thr Gly Ala Ser Thr Leu Val Ile Gly Leu Ala Ser Thr Gln Ala Gln
GGG CCT GGT GAG CCT GCC TTC CTG GGT CCT ACG TTC ACC AAC ACA GGT GCC TTC ACC CTG GTC ATC G|GC CTG GCC TTC ACG CAG GCA CAG

450

460

470

Ser Val Pro Val Ile Asn Ser Met Gly Ser Ser Leu Thr Thr Leu Gln Pro Val Gln Phe Ser Gln Pro Leu His Pro Ser Tyr Gln Gln
AGT GTG CCG GTC ATC AAC AGC ATG GGC AGC AGC CTG ACC ACC CTG CAG CCC GTC CAG TTC TCC CAG CCG CTG CAC CCC TTC TAC CAG CAG

480

490

Exon 7 500 | Exon 8

Pro Leu Met Pro Pro Val Gln Ser His Val Thr Gln Ser Pro Phe Met Ala Thr Met Ala Gln Leu Gln Ser Pro His Ala Leu Tyr Ser
CCG CTC ATG CCA CCT GTG CAG AGC CAT GTG ACC CAG AGC CCC TTC ATG GCC ACC ATG GCT CAG CTG CAG AGC CCC CAC G|CC CTC TAC AGC

510

520

530

His Lys Pro Glu Val Ala Gln Tyr Thr His Thr Gly Leu Leu Pro Gln Thr Met Leu Ile Thr Asp Thr Thr Asn Leu Ser Ala Leu Ala
CAC AAG CCC CAG GTG GCC CAG TAC ACC CAC ACG GGC CTG CTC CCG CAG ACT ATG CTC ATC ACC GAC ACC ACC AAC CTG AGC GCC CTG GCC

Exon 8 540 | Exon 9

550

560

Ser Leu Thr Pro Thr Lys Gln| Val Phe Thr Ser Asp Thr Glu Ala Ser Ser Glu Ser Gly Leu His Thr Pro Ala Ser Gln Ala Thr Thr
AGC CTC ACG CCC ACC AAG CAG| GTC TTC ACC TCA GAC ACT GAG GCC TTC AGT GAG TTC GGG CTT CAC ACG CCG GCA TCT CAG GCC ACC ACC

570

580

Exon 9 | 590 Exon 10

Leu His Val Pro Ser Gln Asp Pro Ala Gly Ile Gln His Leu Gln Pro Ala His Arg Leu Ser Ala Ser Pro Thr| Val Ser Ser Ser Ser

CTC CAC GTC CCC AGC CAG GAC CCT GCC ATC CAG CAG CTG CAG CCG GGC CAC CCG CTC AGC GCC AGC CCC ACA| GTG TCC TCC AGC AGC

600

610

620

Leu Val Leu Tyr Gln Ser Ser Asp Ser Ser Asn Gly Gln Ser His Leu Leu Pro Ser Asn His Ser Val Ile Glu Thr Phe Ile Ser Thr
CTG GTG CTG TAC CAG AGC TCA GAC TCC AGC AAT GCC CAG AGC CAC CTG CCA TCC AAC CAC AGC GTC ATC GAG ACC TTC ATC TCC ACC

630 631

CAG ATG GGC TCT TCC CAG TAACACGCGACCTGGGCCCTGGGCCCTGTACTGGCCTGCTTGGGGGGTGTATGAGGGACGAGCCAGCCCTGCCCTGGAGCCCTGGCCG

AGCAACGGTGGCCCTTCCCTGGACAGCTGTGCCCTGGCTCCCACTCTGCTCTGATGCAACGAAAGGAGAGGCTCTGAGGGGCCCAACCCGTGGAGGCTGCTGGGGGTGCACAGGAGGGG

GTCTGGAGAGCTAGGAGCAAGGCCCTGTTCATGGCAGATGTAGGAGGGACTGTGGCTGGCTTGGTGGGATACAGTCTTCTTACTTGGAACTGAGGGGGCGGCCCTATGACTTGGGCAACCC

CAGCCTGGGCCCTATGGAGAGCCCTGGGACCGCTACACCACTCTGGGAGCCACACTTCTCAGGACACAGGCCCTGTGTAGCTGTGTGACCTGTCTGAGCTCTGAGAGGCCCTGGATCAGCGTGGC

CTTGTCTGTCAACCAATGTACCAACCGGGCCACTCCCTTCCCTGGCCCAACTCCCTTCCAGCTAGTGAACCAATGGCCATTGTACTGACCCCAATCACCCTACTCACAAGGCAATTTCCTGGGT

GCGTACTCTGTGGCAAGGCCCTGGGGCTCTACTGCTCCCTGAGCCACAGGAGGGCCGAGCTAACAGGGAAGGCAAGGCAAGGCTCTCCCTGGGCTTCCCATGCCCAAGCGATTCCCTCTCCCAAGGC

CCCATGACCTCCAGCTTTCCTGTATTTCTTCCCAAGACAATGATGCCCTCTGAGCCCAAGCCCTGGCCCTCCCTGCTCTACTGGGAAGGCTACTTGGGGGCTGGGAAGTGTCCCTTACTCCTGT

GGGAGCCTGGCAACCCGTGGCAAGTCCAGGTTCCCTGGTGGGGGAGCTCCCTGTCTGTCTGAGGGCCCTGGAGACCCCTGGCTTGTTTGGGGCAAGAGTACGTGAGCTCACAAGGCCAAGCAAGGC

CCGAGCAGCTGAGCAGGGCCGGGGAATGGGCCAGCTTGGTGGCCCAAGGAGAGAAAGAGGTGACCCCAAGGGTACCCCAAGGGTGAAGGACTTAACTCAGAGCCCTGGGTG

Table 3. Sequences

CCTGECTGECTGAGGGGAGTTTGGGAGGCAACCTGAGGAGTCTGAGGTCCCTGAGCACTGCGCAGGAGGGAACAAGAGGCTGTGAAACCAAGACAGGCATGGTCCACATCCCTGGGCCCTGC

TGCTGAGAACCTGGGCTTCAGTGTACCGGCTCTACCTGGGATTACGGAAGGCTGGGGTGACCGGGCAACCCCTGCAGCTTGTAAGCAAGCGGGGAGTGGCAGTTTATTAACT

TTTAGTAAAGTCAAGGAGAAATGGGGTGG

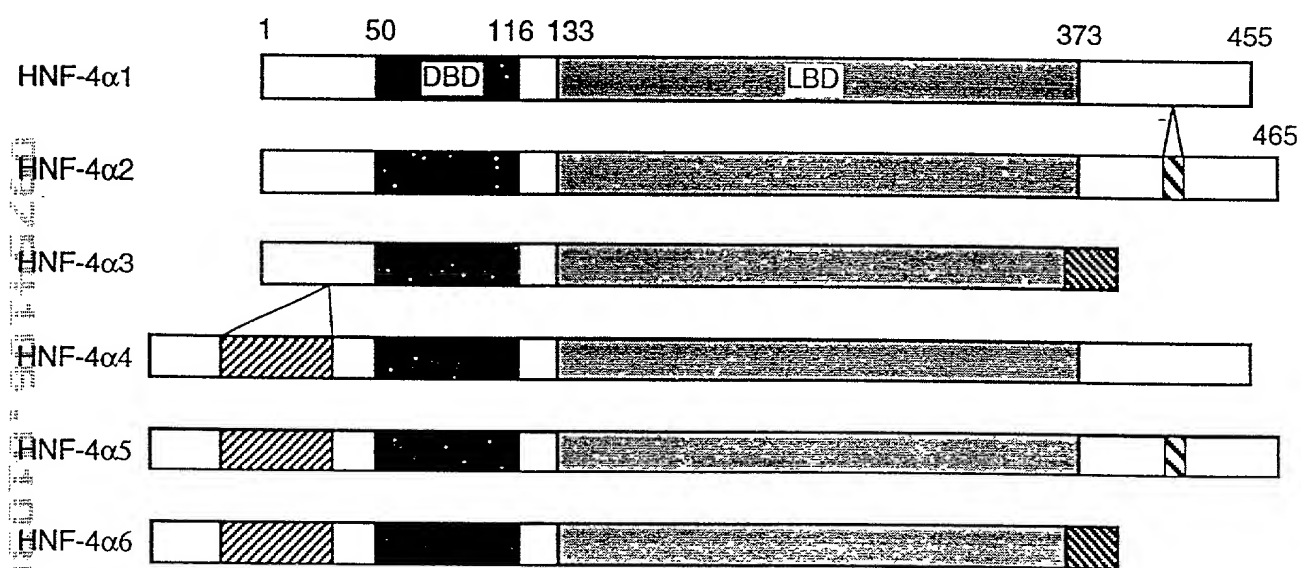
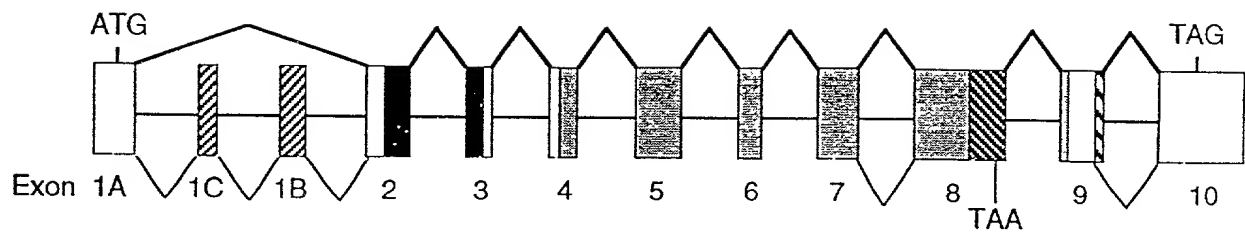


Fig. 12

Fig. 13B

[illegible]

human	G A T C T T C C C A G A G G A C G G T T T G A A A G - - - G A A G G C A G A G G G C A C - T G	1052
mouse	G A G T C T C C C A G A G G A C A G T T T G A A A G A G A G G C A G A G G A C C T G	
human	G G A G G A G G C A G T G G G A G G G C G G A G - - G G C G G G G C C - - - T T C G G	1091
mouse	G G A G A G G C A G A G G A G G G C G G G A C G G G G G C T G G G C T C A G C C A G	
human	G G - - - T G G G C G - - - C C A G G - - - G T A G G G C A G T G G C C G C G G C G T G G A	1130
mouse	G G G C T T G G G T G G C A T C C T G G G C C G G G C A G A C A G G G G G C T A A G G C G T G G G	
human	G G C A G G A A T G C G A C T C T C C A A A A C C C T C G T C G A C A T G G A C A T G	1176
mouse	T A - G G G G A G A T G C G A C T C T C T A A A A C C C T T G C C G G C A T G G A T A T G	

F. 4. 13C

125	126	127	128	129
G C G G	G A C	C G G	A T C	A G C A
Arg	Asp	Arg	Ile	Ser

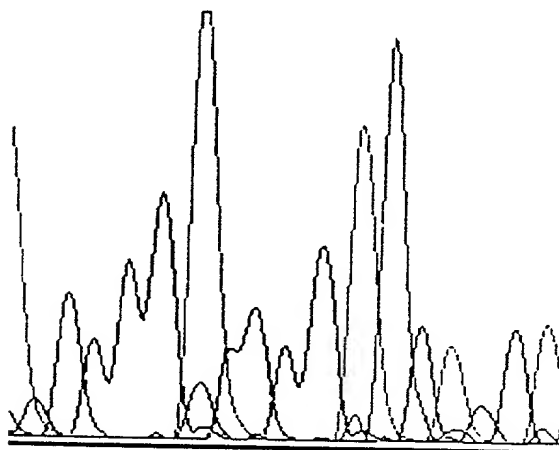


Fig. 14A

G C G G G A C T G G A T C A G C A
Trp

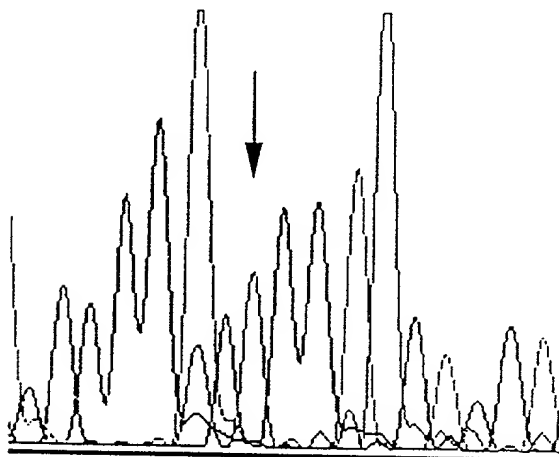
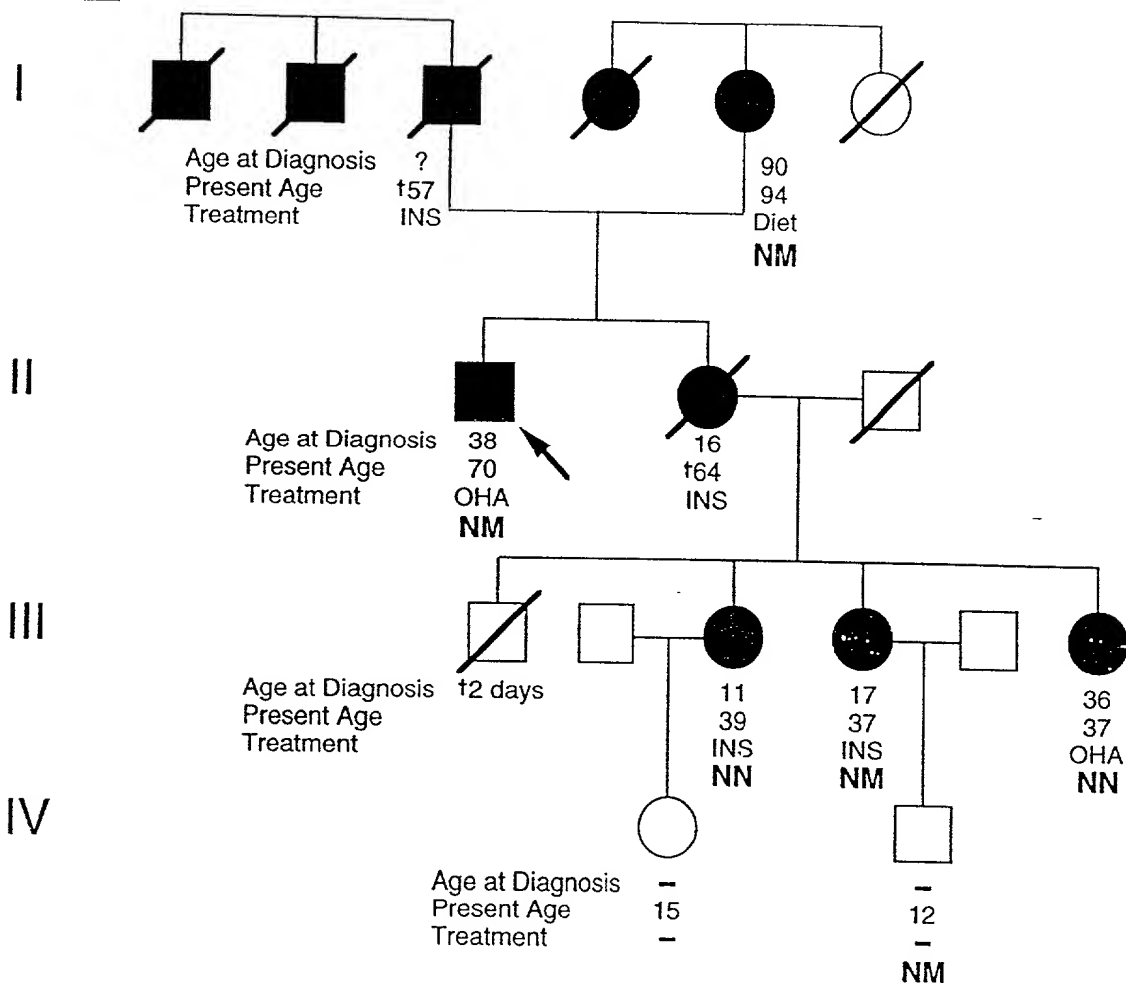


Fig. 14B

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J2-21



J2-96

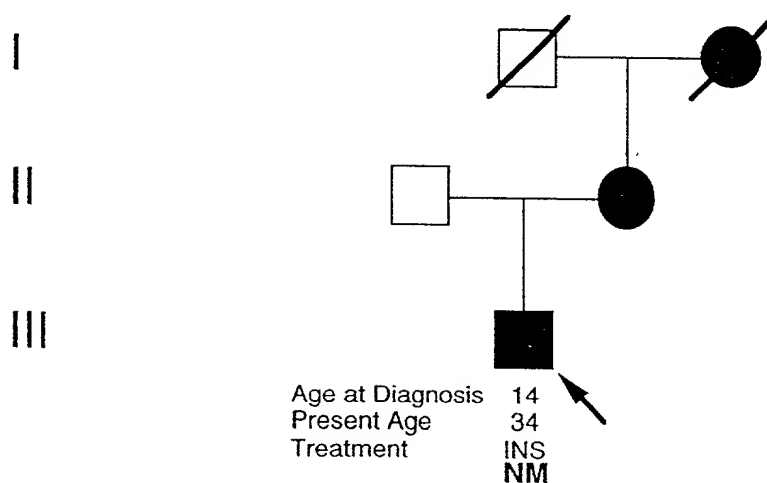


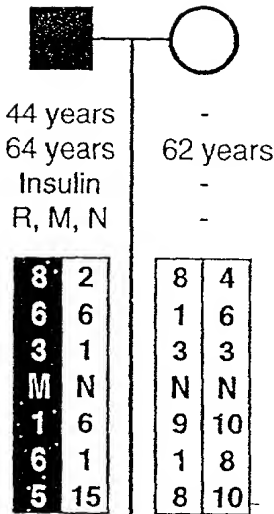
Fig. 15

Fig. 16

I

Age at Diagnosis
Present Age
Present Therapy
Complications

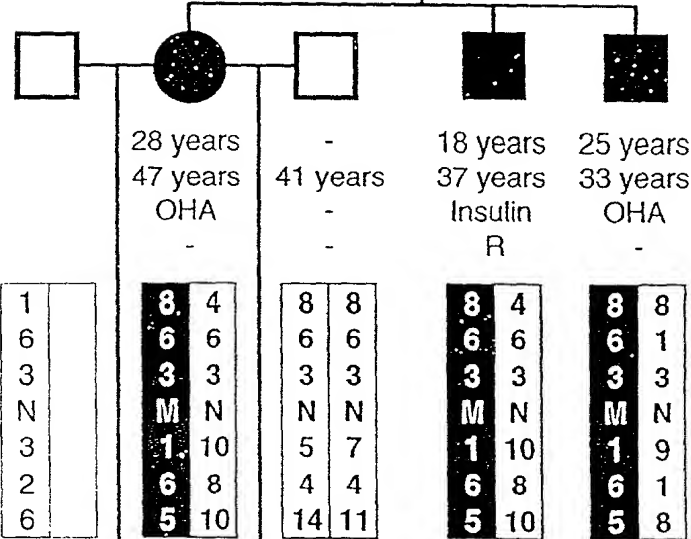
D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424



II

Age at Diagnosis
Present Age
Present Therapy
Complications

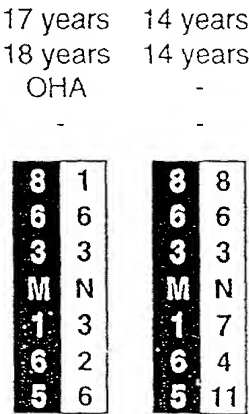
D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424



III

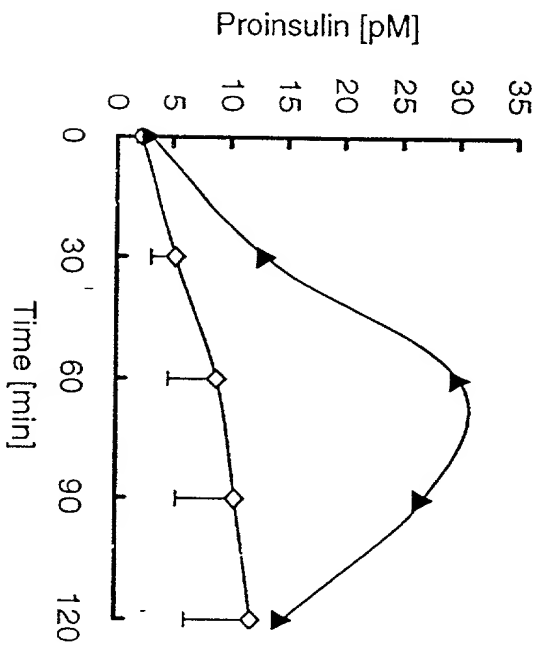
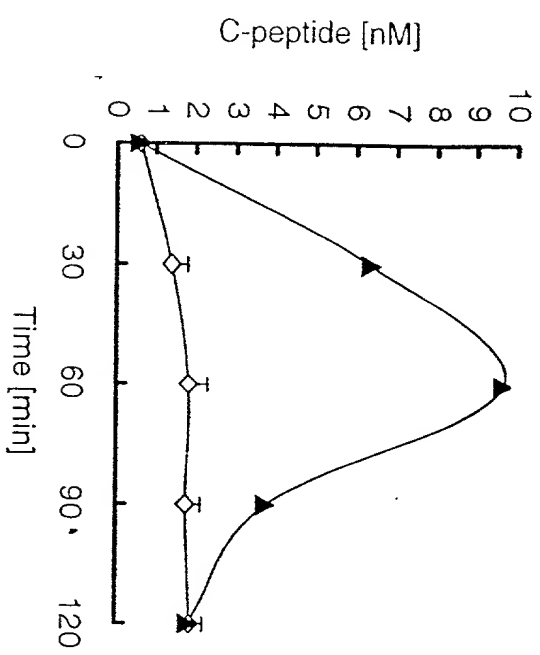
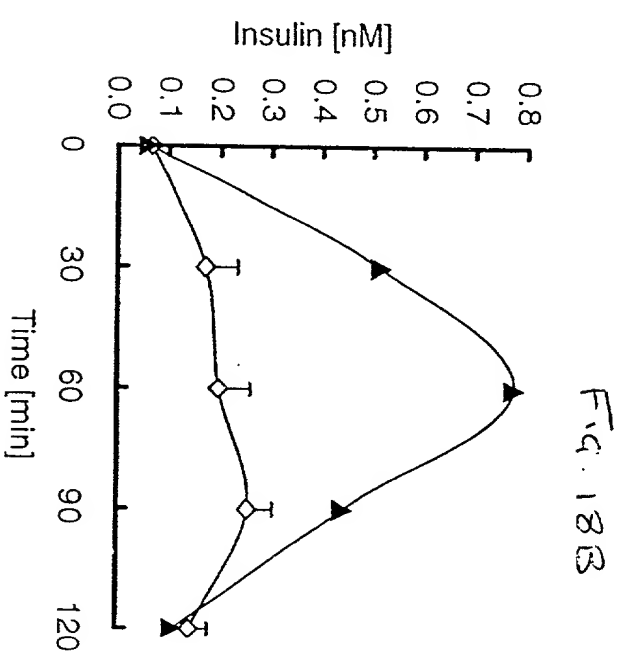
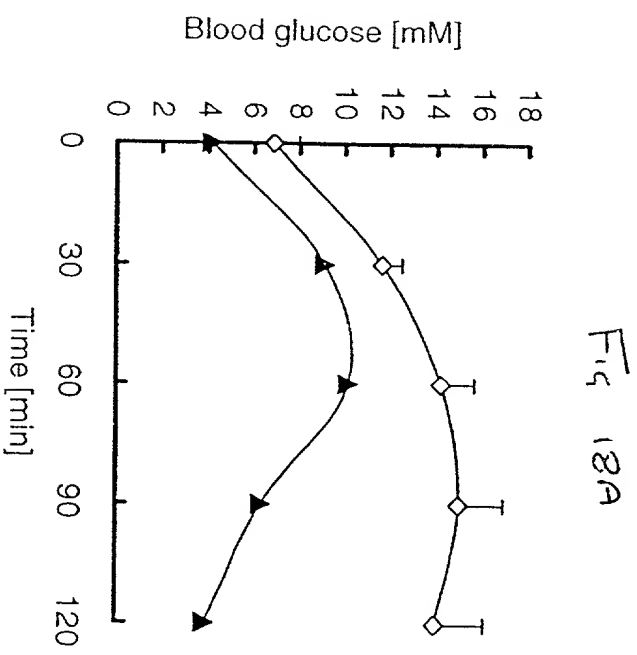
Age at Diagnosis
Present Age
Present Therapy
Complications

D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424



Ala Glu Val Leu Ser Arg Gln |
Stop
G C G G A G G T C T G T C C C G A C A G G T A C C G G G G

Fig. 17



09754106-010301

Fig. 19A

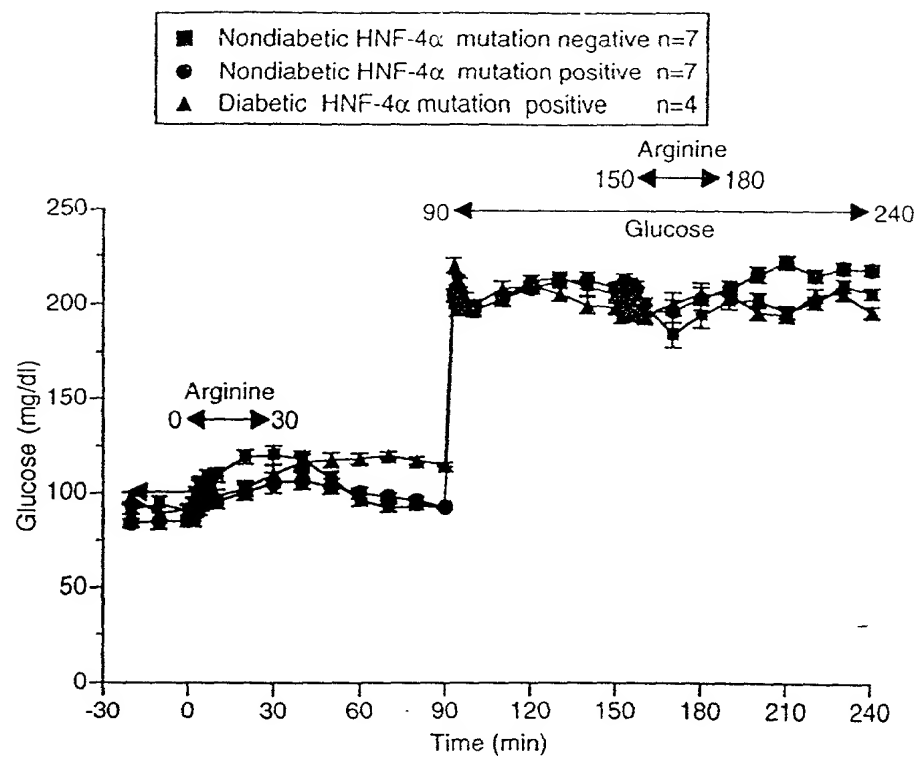
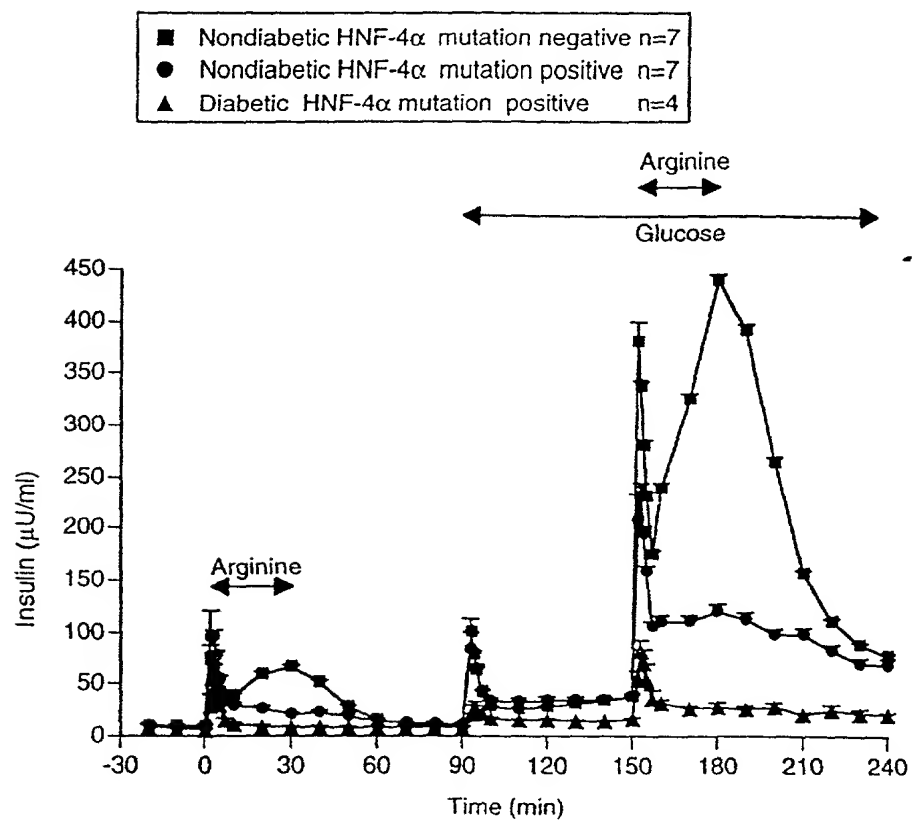
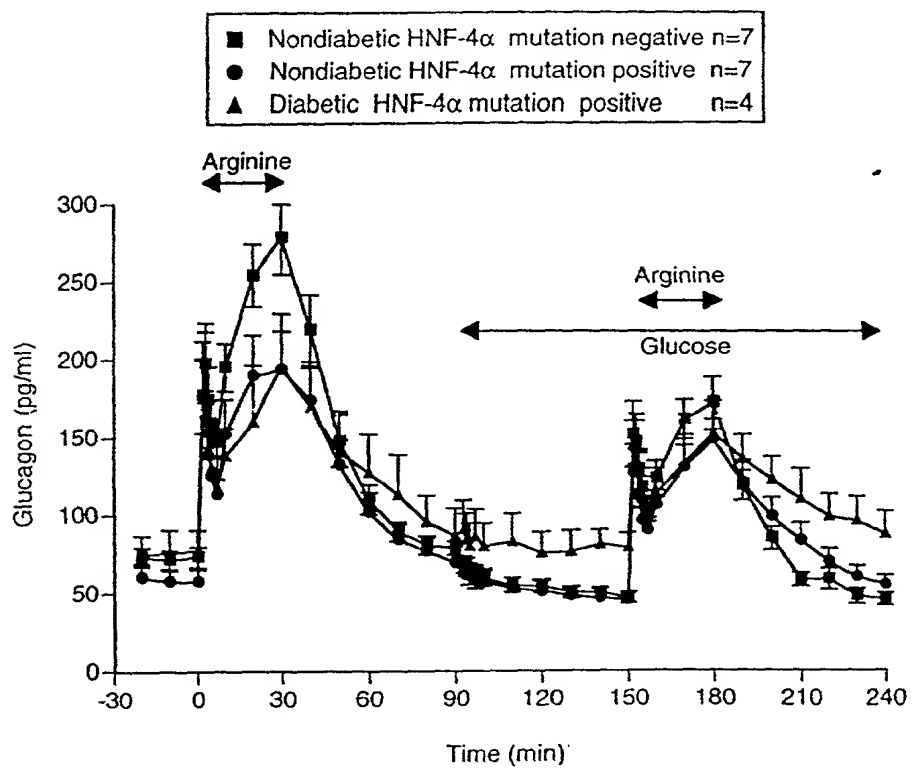
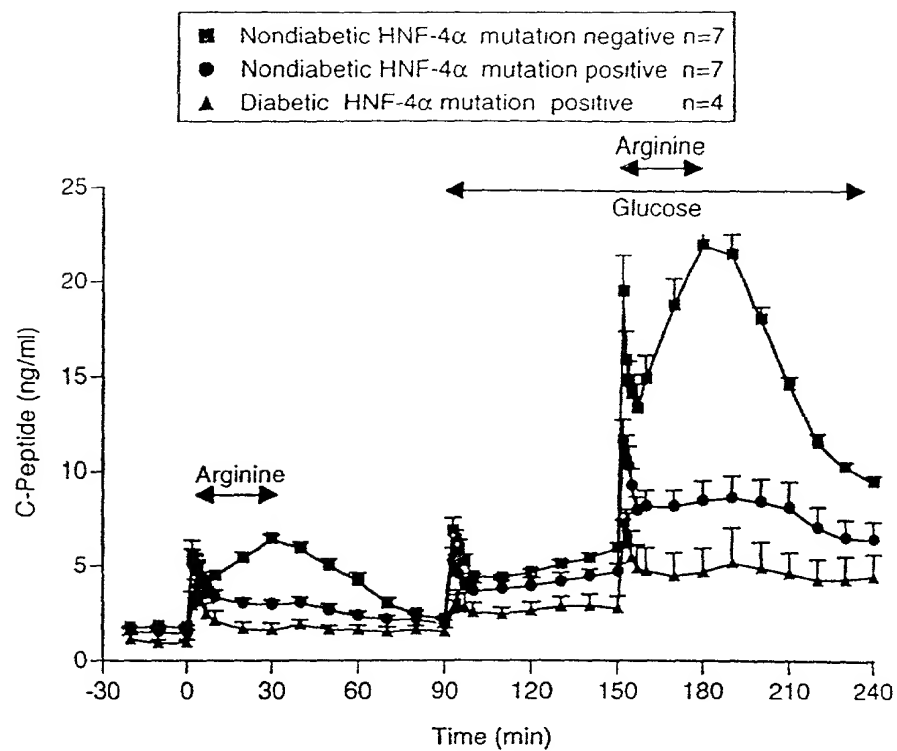


Fig. 19B



[illegible]

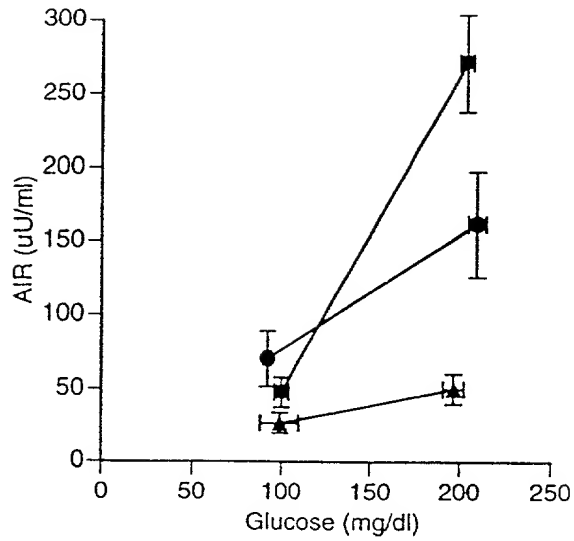
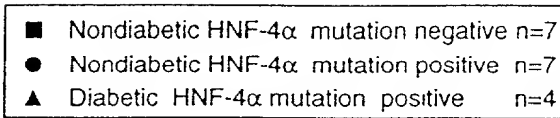


Fig. 20A

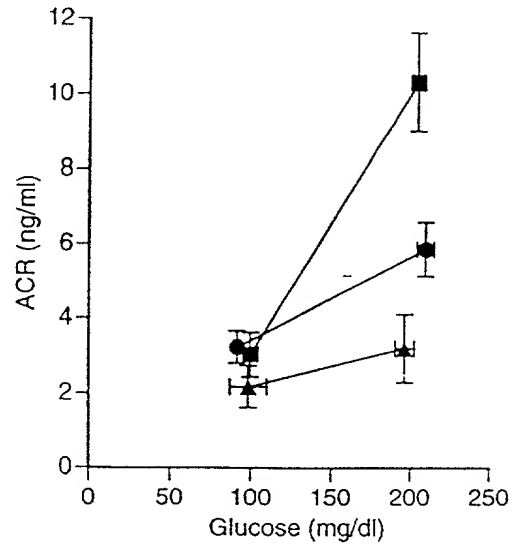


Fig. 20B

11



D12S321
D12S76
UC39

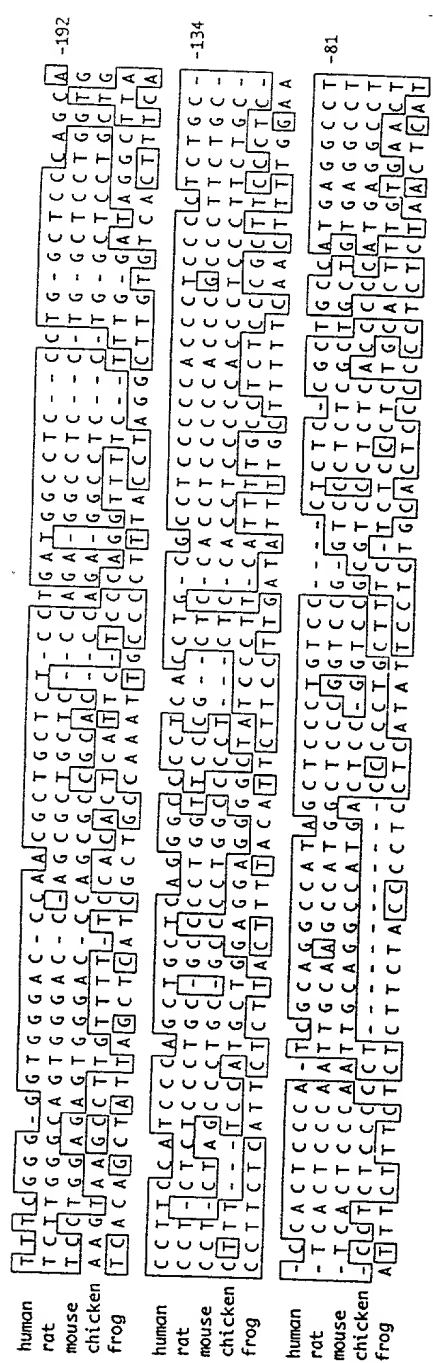


Fig. 22A

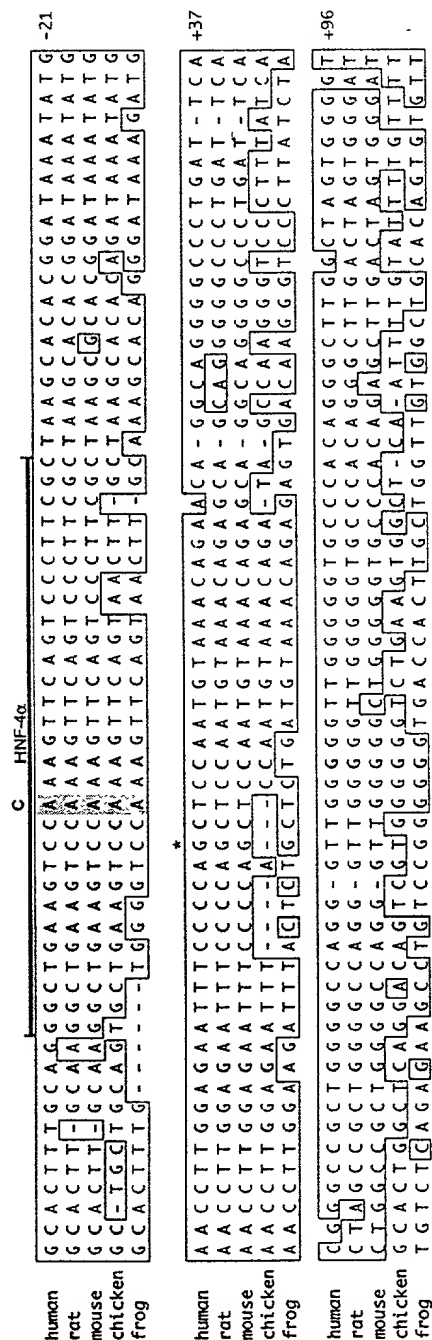


Fig. 22B

Fig. 22C

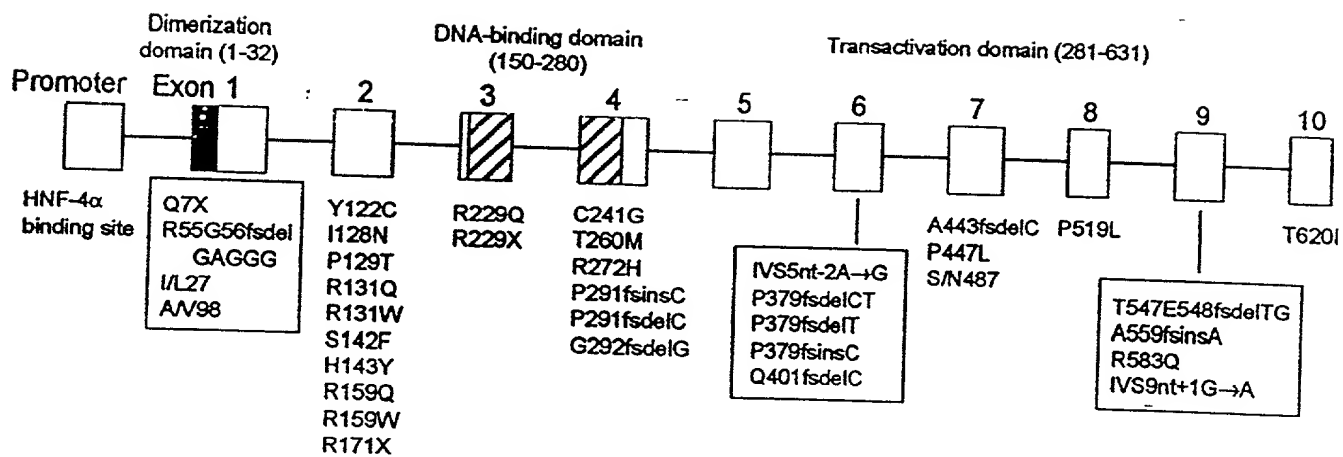


Fig. 23

J2-20

175	176	177	178		
A	AAG	CAA	NGA	GAG	AT
	K	Q	R	E	
			X		
			C/T		

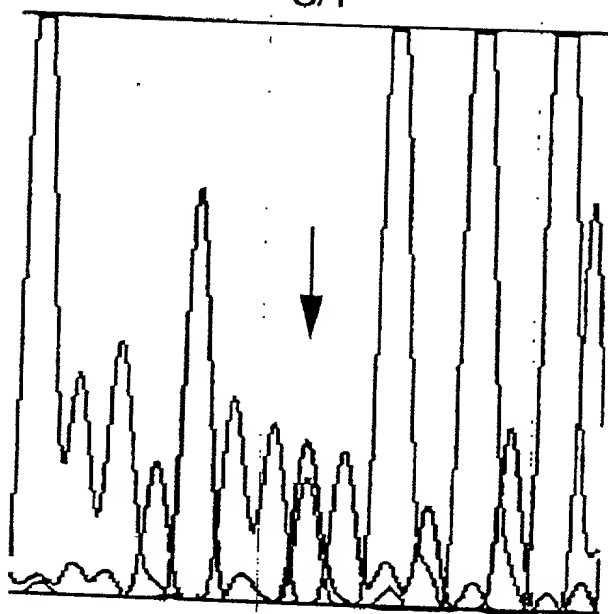


Fig. 24

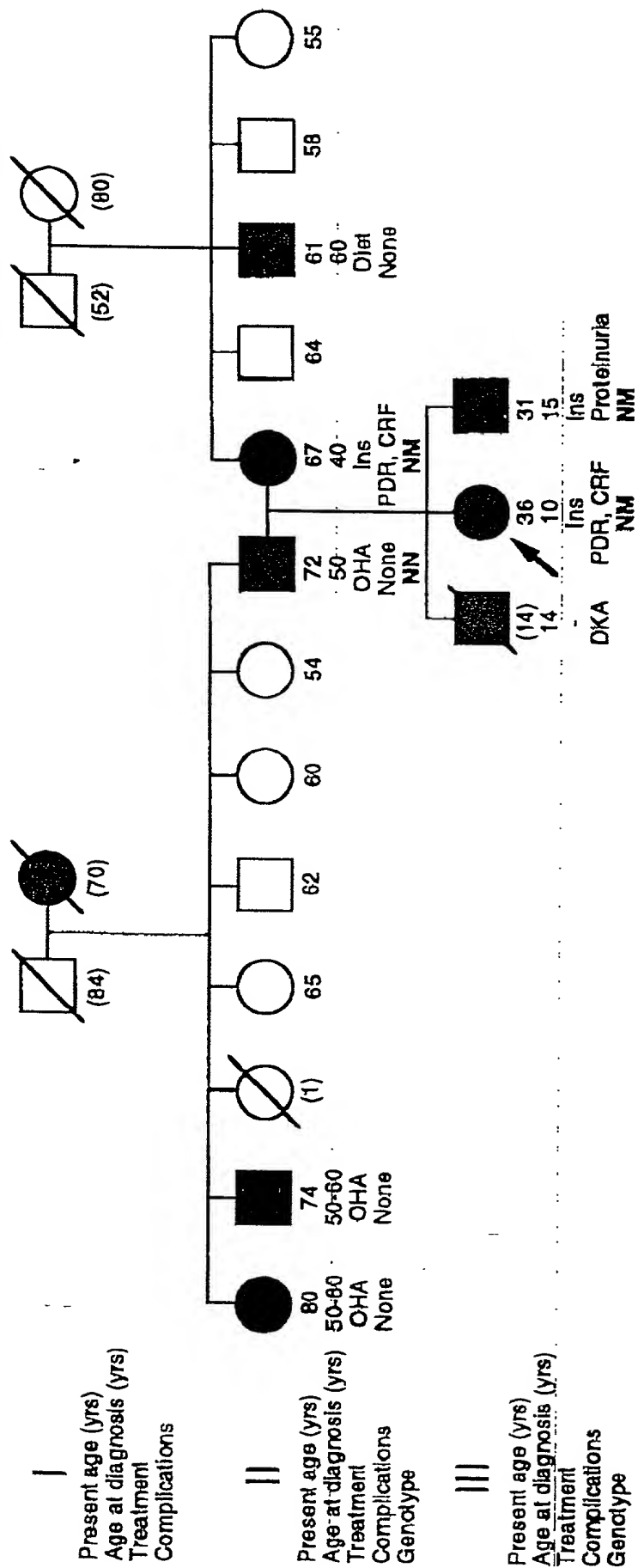


Fig. 25

1 AGCCAGCACGTGTTCTTGGCACATGGTAATCTTAACATATTTTTCCTACAGGAGGCCCTGGTGTCAAGCCCGGAGTGGGGTGGAAAGGTC
 NF1 HNF-3 AP1
 91 CCAAAATGGATGGAAGGGCCCCAAATGGCCGTGAGCATCCCTCTGCCCTTGAGAAAGAGCTAGCCCAAGCTGTCTAGAGCTCCCTGCTGCTG
 NF1 AP4
 181 CCGCTCTCGTAAGCAGCAAGCAATTTTGGCTCTCCTGTCTCAGCATGATGCCCTTACAAAGGTTCTTTTCGGGGGTGGGACCCAAACGCTGCT
 NF1 AP4
 271 CTCCTGATGGCCTCCCTGGCTCCAGCACCCCTCCATCCAGCTGCTCAGGGCCCCCTCACCTGCGCCTCCCCCAACCTCCCCCTCTGCCCCAC
 NF1 AP4 HNF-4α
 361 TCCCATCGCAGGCCATAGCTCCCTGTCCCTCTCCGCTGCCATGAGGCCCTGCACCTTTGCAAGGCTGAAAGTCCCAAGTTCAAGTCCCTTCGCT
 NF1 HNF-3 C/EBP * Exon 1 HNF-3 AP1
 451 AAGCACACGGATAAATATGAACCTTGGAGAAATTTCCCCAGCTCCCAATGTAAACAGAACAGGCAGGGGCCCTGATTCAAGGGCCCGCTGGGG
 541 CCAGGGTTGGGGTTGGGGTGCCACAGGGCTTGGCTAGTGGGGTTTGGGGGGGCGAGTGGGTGCAGGAGTTTGGTTTGTCTGCTGCCG

FIG. 26A

631 GCCGCGAGGCAAAACGCAACCCACGCGGTGGGGGAGCGGCTAGCGTGGTGGACCCGGGGCGCGTGGCCCTGTGGCAGCCGAGCCATGGTT^{MetVal}
 SerLysLeuSerGlnLeuGlnThrGluLeuLeuAlaLeuLeuGluSerGlyLeuSerLysGluAlaLeuIleGlnAlaLeuGlyGlu^{Leu}
 721 TCTAAACTGAGCCAGCTGCAGACGGAGCTCCTGGCGGCCCTGCTCGAGTCAGGGCTGAGCAAAAGAGGCACTGATCCAGGCACTGGGTGAG^G
 ProGlyProTyrLeuLeuAlaGlyGluGlyProLeuAspLysGlyGluSerCysGlyGlyGlyArgGlyGluLeuAlaGluLeuProAsn
 811 CCGGGGCCCTACCTCCTGGCTGGAGAAAGCCCCCTGGACAAAGGGGAGTCTCGCGCGCGGTCCGAGGGGAGCTGGCTGAGCTGCCCAAT^C
 GlyLeuGlyGluThrArgGlySerGluAspGluThrAspAspGlyGluAspPheThrProProIleLeuLysGluLeuGluAsnLeu^{Val}
 901 GGCTGGGGGAGACTCGGGGCTCCGAGACGAGACCGATGGGAAGACTTCACGCCACCCATCCTCAAAGAGCTGGAGAACCTC
 SerProGluGluAlaAlaHisGlnLysAlaValGluThrLeuLeuGln(n)109
 991 AGCCCTGAGGAGGGGGCCACCAGAAAGCCCGTGGTGGAGACCCCTTCTGCA gtaaggagccctgccccgtccccgagagagagccta^T

FIG. 26B

gaggggccccctcagctcctaacagagcccccttctgagttgagtgctcccatgaccttcagcctttagcctagttgctgggaagggggac
agggcccatgagagccaggggtccttgcttgagggtttgagcctccagccccctgaactgctcctctgcagaggtcccaaatcccatgagc
ccaggcccttagcccgagtccttggnagggggacatttcccaggggtcccaagatggggagaaaaagcagtgaaattcacaaactcaaatgc
c::::: 9 kb ::::: caccacccatccatccatccgtccatccacccattcatccattcatccatccatccatccatcc
acatatcttcattctgtgtgtgtgtgtatccatgtttctaaacctttatctgttccagtgctgtatccatagggcctgtgtccacg
tttgtcatgtgtgtgcgtcnacaaagtctctgtcctcatgacctgtgtgtgtgtgtcctgtgtcctgggcataaaatgaccataacctaccgt
ccctgagtcctatgtgtaggccccctgggtcccataaactgctttcatgcacagtccccacccctcagagttgacaagggttccagcaccacaggga
cgcagccccacctatggggagagacagcccccttgctgagcagatccccctcttgcctctccccag GGAGGACCGGTGGCGTGTGCCGAAG

FIG. 26C

1801 MetValLysSerTyrLeuGlnGlnHisAsnIleProGlnArgGluValValAspThrThrGlyLeuAsnGlnSerHisLeuSerGlnHis
 ATGCTCAAGTCCTACCTGCAGCAGCACACATCCACAGCGGGAGGTGGTCGATACCACTGGCCTCAACCAGTCCCACCTGTCCCCAACAC
 A (R131Q)
 1891 LeuAsnLysGlyThrProMetLysThrGlnLysArgAlaAlaLeuTyrThrTrpTyrValArgLysGlnArgGluValAlaGlnG (ln) 176
 CTCACAAAGGGCACTCCCATGAAGACGACGAGAGCGGCCCGCTGTACACCTGGTACGTCGCCAAGCAGCGAGAGGTGGCGCAGC gtaag
 1981 taatgaccctaccccgcatcttccctggaggggcccgagactctcccctaactcataggtgggggctggaagcttcaccatccccattac
 2071 acagacaggtagatggaaaggaagtcagtgaggattcaacctgcattttattacattcttgcgccagggcactctgtgggacgggagtanac
 2161 ttggtcctgaacatccaaagatgaatgaaatgggtccctgcttcttttttttttagata::::: 3.8 kb :::::cgtagact
 2251 ctggaaaaaatatgtaagctctctgagcctcagcttcttctcatctgtacaaatggggatagtaaaatgtgcaaaatcagaacaaatgctaatgc
 2341 ttacctgcagtcctgtactgagaaggatggtgagatcatatctctgggttaggaagcatttcagggattgattagtgatgtttgcctt

FIG. 26D

2431	gaacacaggttaagaaagtgatggcatgtgtgtgtgttctgtcatcagtagatttctaagttcttagctgtaagctcctct
2521	ggttcagcgccatggcaatgagaaagaatcaaggccaaggtcagggaatggacaggaaggtgagagtggccagtagccccactcacgg
2611	Exon 3 176 (g)lnPheThrHisAlaGlyGlnGlyGlyLeuIleGluGluProThrGlyAspGluLeuProThrLysLysGlyArg ctttctgtgcctgcag AGTTACCCCATGCAGGCAGGGGGCTCATTTGAAGAGCCACAGGTGATGAGTACCAACCAAGAGGGGCGG
2701	ArgAsnArgpHeLysTrpGlyProAlaserGlnGlnIleLeuPheGlnAlaIleArgGlnLysAsnProSerLysGluGluArgGlu AGGAACCGTTTCAAGTGGGGCCAGCATCCAGCAGATCCTGTTCAGGCCCTATGAGAGGCAGAGAACCCTAGCAAGGAGGACCGAGAG
2791	ThrLeuValGluGluCysAsnAr (g) ²³⁸ ACGCTAGTGGAGGATGCAATAG gtacaacggcggcgcggaacagtgctgtgttctggtcgtcggaagggccaggggaaggggaag

FIG. 26E

2881 gtgactctaggctcctgtaaaaggctgtccagttg^cccgagaactcctgatattggcttagcctgcccagaaaaattgagaataacttgaacc

2971 taagcccatctctcgagccccccctgcacntggacaccaagcaaccccttccatggatgctcacccaattogatttctctacaatcct

3061 atggctcttttgcctcaactttatgaatggagagactgaggtcagacagactgtcaattgcccaggtcacacacagacacctggcattggaa

3151 cccagatctgccagcctcaaacctccggcagagntcagcttctcagaacctcccccttcatgcccaggacaggggttccctctgagcctgg

3241 cctggaggctcatgggtggctatttctgcag GCGGAA^{Exon 4} 238 (Ar)gAlaGluCysIleGlnArgGlyValSerProSerGlnAlaGlnGlyLeuGlySerAsnL
G(C241G)

3331 euValThrGluValArgValTyrAsnTrpPheAlaAsnArgArgLysGluAlaPheArgHisLysLeuAlaMetAspThrTyrSerG
TCGTCACGAGGCGTGTCTACAACCTGGTTTGGCAACCCGGCGCAAGAGAGCCTTCCGGGCACAAGCTGGCCCATGGACACGTACAGCG
A(R272H)

FIG. 26F

3421 lyProProGlyProGlyProAlaLeuProAlaHisSerSerProGlyLeuProProAlaLeuSerProSerLysValH
 GGCCCCCCCCAGGCCAGGCCGGACCTGCGCTGCGCTCACAGCICCCCTGGCTGCTCCACCTGCCCTCTCCCCCAGTAAGGTCC
 C (P291fsinsC)
 isG(ly) 319
 3511 ACG gtaagtgtatgtgggacaaaggacacgtgggaaggtgggaggttgggaggaactgtccattgacagcagtcacctaaccctct
 3601 ttgcacgtcagtttggttccattc::: 2 kb ::::gcagctgacccaggattggcaaaaggtagaaacaaaggcagattt
 3691 gctggctgcataaaaggcagacagggcagatggcctaagcaaaccaatggagtttgaagtgtctgagggctgtggaggcaggggagggcaggg
 Exon 5 319 (G)lyValArgTyrGlyGlnProAlaThrSerGluThrAlaGluValProSerS
 3781 aagtgggtgtctgaggcaggacactgcttccctctccag GTGTCGCTATGGACAGCCTGCGACCACTGAGACTGCAGAGTACCTCAA
 erSerGlyGlyProLeuValThrValSerThrProLeuHisGlnValSerProThrGlyLeuGluProSerHisSerLeuLeuSerThrG
 3871 GCAGCGCGGTCCCTTAGTGACAGTGTCTACACCCCTCCACCAAGTGTCCCCCACGGGCTGGAGCCCCAGCCACAGCCTGCTGAGTACAG

FIG. 26G

3961 luAlaLysLeu³⁶⁹
 AAGCAAGCTG gtgagtgtccttgcttgaaggaaacccaaacctcatcttcccttgccaggagattctggagcagtccttagggaggc
 4051 cctgtgggacccccggccccccggacacagcttggtcttccccctcgtag GTCTCAGCAGCTGGGGGCCCTCCCCCTGTCTCAGCACCCCTG
 ThrAlaLeuHisSerLeuGluGlnThrSerProGlyLeuAsnGlnGlnProGlnAsnLeuIleMetAlaSerLeuProGlyValMetThr
 4141 ACAGCACTGCACAGCTTGGAGCAGACATCCCCAGGCCCTCAACCCAGCAGCCCCCAGACCTCATCATGGCCCTCACTTCCTGGGGTCAAGACC
 (P379fsdelCT)
 (IVSnt-2A-G)
 (Q401fsdelC)

FIG. 26H

IleGlyProGlyGluProAlaSerLeuGlyProThrPheThrAsnThrGlyAlaSerThrLeuValIleG(ly)⁴³⁷
 4231 ATCGGCGCTGGTGAGCCTGCCTCCCTGGGTCTACGTTCCACACAGGTGCTCCACCTGGTCATCG gtaagctgggtggggatgggt
 4321 gggcacctgggtgggaggctcatggggcaaccgcanaatccaggagctggaaaagccactgggactcattcattcattcattc
 4411 caacatgt::::: 0.8 kb :::::taggagaggggagcagagaactgaccccatggcctttgcaactgctgtgtgtacccagggctc
 4501 cagggaaccgcagtttgacaacttttgacaagtcccgcttgcttttccattagcttagacaaaagagctaaaggctcagagaggggga

Figure 1 continues on the next page

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FIG. 26I

FIG. 26J

lnSerProHisA(1a)⁵⁰¹
 4951 AGAGCCCCACG gtgagcaccctgtgccccacacagcaggagatgatgatagaggttggtgtcaatggatgcagggaaaggggtgcct
 5041 ggcaggcattgcagctgtctctctgggacaagtgtgtttccgtgattgaggggtgtctgcaggccagtggttcccatgtgaatgc
 5131 acgtatctgtgtgtgcacgactgtgtgtgagcagatccctagtgcgtgtctctgggtgtgtatcggttgcatttgggtgcatt
 5221 gcctgtgtttctctgaaactcttagggcccatatgaatttctaaaaatctattcaga:::: 1.5 kb ::::ccagttttgaaaaatc
 5311 agccttgggatctccaactgctgcccagctctggctgttcagcaggcccccatgccccctttccccagtccttgaggcctgggactagggtg

FIG. 26K

5401 tcaggcacgtttgccacgtctgtccctctctccctgaggccag CCTCTACAGCCACAAGCCGAGGTGGCCAGTACACCCACACGGG
Exon 8 501 (A) laLeuTyrSerHisLysProGluValAlaGlnTyrThrHisThrGln
A
5491 yLeuLeuProGlnThrMetLeuIleThrAspThrThrAsnLeuSerAlaLeuAlaSerLeuThrProThrLysGln⁵⁴¹
CCTGCTCCCGCAGACTATGCTCATCACCAGACACCAACCTGAGCGCCCTGGCCAGCCTCACGCCCCACCAAGCAG gtaagggtccaggcc
Exon 9 542ValPheThrSe
5581 tgctggccctccctcggcctgtgacagagccccctcacccccacatccccggggtcaggaggctgtctctgtctccccag GTCTTACACCTC
rAspThrGluAlaSerSerGlyLeuHisThrProAlaSerGlnAlaThrThrLeuHisValProSerGlnAspProAlaGlyI
5671 AGACACTGAGGCCGCCAGTGAGTCCGGGCTTCACACGCCCGGCATCTCAGGCCACACCCCTCCAGTCCCCAGCAGGACCCCTGCCCGGCAT
(T547E548fsdelTG)

FIG. 26L

eGlnHisLeuGlnProAlaHisArgLeuSerAlaSerProThrV(al) 590
 5761 CCAGCACCTGCAGCGGCCACCGGCTCAGCGCCAGCCCCACAG gtgagaggccctgggtccacccccctcccttactgtccctgccccct
 a(IVS9nt10-A) t
 5851 tccatgttggtcccccccccttctgtgtgctgctcactgtggggtgtgcatgcagcagccctagggctgtgtgaggaagcactggca
 5941 ggcgtggaagggtgggtggcttccatgaa::: 1.5 kb ::::: tccagtgttcacagtaagatgtactcagggccagtcctcatgg
 6031 gcggccgtggaccctggctggaggctccctttgttaagaaccaggggtagaggtgtgactttgggttccctgttatgtgtgatcca
 6121 ggaggtgtggccctgcctccccatcctgagtaccctagggacagggcaggtgggtgtgggtgcctgtgggtgggtgtagcagcctt
 c
 Exon 10 590 (V) alSerSerSerSerLeuValLeuTyrGlnSerSerAspSerSerAsnGlyGlnSerHisLeuLeuProSerAsnHi
 6211 gtttgcctctgcag TGTCTCCAGCAGCAGCCTGGTGTACCCAGAGCTCAGACTCCAGCAATGGCCACAGGCCACCTGCTGCCATCCCAACCA
 sSerValIleGluThrPheIleSerThrGlnMetAlaSerSerSerGlnOc631
 6301 CAGCGTCATCGAGACCTTCATCTCCACCCAGATGGCCTCTTCCTCCCAGTAACCCACGGCACCTGGGCCCTGGGGCCTGTACTGCCCTGCTT
 6391 GGGGGGT

FIG. 26M

PrF
CATGAACCCGGAAGAGTAGTCTCTCTGGACTAAAGCGGAACGTAGAACCCGCGCTAGGCTGCAAGGCTGGCTTAAACAGTCCAAAGGTTAGGTGAAGTTT
GGCTGATTAAGCAGAACCAAGTAAAGAGGTCTCTAGCCCCCAGCGTGAATGACCCCTGGCAAGCCCGCTCCGCGCCAGGCTCTTCTGCTCTCCAGGCTCTGCCCTCCGGCTCT
CCCCTCTCTCCGGGTTTCCCGCTCCCGCCACCATCATTTGTCATCCAGCGAAAGCTGGCGCTTCCCACTAATTGTCATATCTTATGCGCTAATGGTGGCGATCATGGCAAGTT AGAAG
TTTTCTGACTCTTTTCGGAGGAGCTCCCGGACCCCGGGGAGTACAGGTCTGTGGAGCGTGAAGGCTGGAGGGTTCTCTGGATTGCGGTTTGGGTTTGGCTTGTGAACCTCCCTCCACCTCTC
TCTCGCACCCACCCCTCACCCCTCTCTTTTTCGTCCTTTGAAA
Ser Ser Gly Val Thr Lys Glu Val Leu Val Gln Ala Leu Glu Glu Leu Leu Pro Ser Pro Asn Phe Gly Val Lys Leu Glu Thr Leu Pro
AGC TCC GGG GTC ACC AAG GAG GTG CTG GTT CAG GCC TTG GAG GAG GTG CTG CCA TCC CCG AAC TTC GGG GTG AAG CTG GAG ACG CTG CCC
Leu Ser Pro Gly Ser Gly Ala Glu Pro Asp Thr Lys Pro Val Phe His Thr Leu Thr Asn Gly His Ala Lys Gly Arg Leu Ser Gly Asp
CTG TCC CCT GGC AGC GGC GGC GAG CCC GAG ACC AAG CCG GTC TTC CAT ACT CTC ACC AAC GGC CAC GCC AAG GGC CGC TCG TCC GGC GAC

PrR
Met Val Ser Lys Leu Thr Ser Leu Gln Gln Glu Leu Ser Ala Leu Leu
ATG GTG TCC AAG CTC ACG TCG CTC CAG CAA GAA CTC CTG AGC GCC CTG CTG

Exon 1
Exl-1F
Exl-2F

1

FIG. 27A

FIG. 27B

[illegible]

Met Arg Arg Asn Arg Phe Lys Trp Gly Pro Ala Ser Gln Gln Ile Leu Tyr Gln Ala Tyr Asp Arg Gln Lys Asn Pro Ser Lys Glu Glu
 ATG CGC CGC AAC CGG TTC AAA TGG GGG CCC GCG TCC CAG CAA ATC TTG TAC CAG GCC GAT CGG CAA AAG AAC CCC AGC AAG GAA GAG
 270
 Arg Glu Ala Leu Val Glu Glu Cys Asn Ar (g)
 AGA GAG GCC TTA GTG GAG GAA TGC AAC AG GTAACACACACAGAGCTCAGTGGGAGGTGGGCAAGTACACAGACCCAGGAACCCCTCCCTCGGTCTCGGATATTGACA
 EX3R
 CACTAGTTATACAGATAAGTGTGGCTAAATCAGAGCTTCTCAAAAGTATGTCCACA::: 2 kb :::::CTGATTGTGTGTTTTTGGGCCAAGCACCACCAAGTCCCGCGCCCC
 EX4-1F
 270
 Exon 4 (Ar)g Ala Glu Cys Leu Gln Arg Gly Val Ser Pro Ser Lys Ala His Gly Leu Gly Ser Asn Leu Val
 CCTTCACTACCATCTCCCTCCATCCATCCATCCAG G GCA GAA TGT TTG CAG CGA GGG GTG TCC CCC AAA GCC CAC GGC CTG GGC TCC AAC TTG GTC
 EX4-2F
 Thr Glu Val Arg Val Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu Glu Ala Phe Arg Gln Lys Leu Ala Met Asp Ala Tyr Ser, Ser Asn
 ACT GAG GTC CGT GTC TAC AAC TGG TTT GCA AAC CGC AGG AAG GAG GAG GCA TTC CGG CAA AAG CTG GCC ATG GAC GCC TAT AGC TCC AAC
 349
 Gln Thr His Ser Leu Asn Pro Leu Leu Ser His Gly Ser Pro His His Gln Pro Ser Ser Pro Pro Asn Lys Leu Ser G (ly)
 CAG ACT CAC AGC CTG AAC CCT CTG CTC TCC CAC GGC TCC CCC CAC CAG CAG CCC AGC TCC TCT CCT CCA AAC AAG CTG TCA G GTAAGCAAAGGT
 G K Q R

FIG. 27D

EX4-1R

TGGGCTCACTGCTCGGCAACCAACATCCTGTTCTTGCACAGGATCTTATCTGTTTAAAGGTTTTCAGAGGAGCAAAACGCTTTTGAGATGATCCTTAGGGCCGCTCTCTCATTTGCCA
 L G L T A S A T Q P S W F L P R I L S G L R V F R G A N A F E M I L G P L S H C Q
 GAATATACTCCCTCGGAATAATGTGTGGCTCTGATCAGTT:..... 3 kb ::::CCAGGCACTGGGGATACATCAGTGAACAAAACAAACGAGATAAAAATTTCTCCCTCCCTCGTG
 N I L P W K O C
 399

GCCTTACATTTAGAAATTAATAGAGACATGCCATATTTACCTCGGAGAAAGCAGCCGATATTTCTTGTGGTGGACAGGGGAGGAGAAACGAACTTTTATTCTTATTACCCACCTT
 349

EX5F

TGAAACAAGAGGTGCGGAGTCATTGTTCCAGGACCCCTGGTGGCACAATGTTCCCTACTGGGTTTGTGTTTTCAG GA GTG CGC TAC AGC CAG CAG GGA AAC AAT
 Glu Ile Thr Ser Ser Thr Ile Ser His His Gly Asn Ser Ala Met Val Thr Ser Gln Ser Val Leu Gln Gln Val Ser Pro Ala Ser
 GAG ATC ACT TCC TCA ACA ATC AGT CAC CAT GGC AAC 402
 Leu Asp Pro Gly His Asn Leu Leu Ser Pro Asp Gly Lys Met

EX5R

CTG GAC CCA GGC CAC AAT CTC CTC TCA CCT GAT GGT AAA ATG GTGATACACCTGGGCCATTGTCGCTCTGGAGCTGATAAGATAAGAGGCAAAACAAACAACTT
 CTCACAAGGCTGCCCTCAAAACAATGRACCATTTGTAGCCCCATAGGGGAAATGAGGGCTGTCCAGAGTCGGAAGGAGAGGTAGTGTGCTGAGCCACCCCTTTGGCGGGTAGAAAA: : : :
 : : : : 5 kb : : : : CCCAAAGTGATGGGATTACAGGGGTCAAAGCACCATGCCCAATTAATTGTATTGAGTGAATGAAGGAATGAATTTGAGAACTAGTCATGCCAAGGAATCGCTA

FIG. 27E

403
 EX6F
 AGTCACATCGTTGGAAACTGCTCTTTTGGGTCCAAAGTCCACCCATGTTTCTCTCTTGTGTTTCTCTCCATCAG ATC TCA GTC TCA GGA GGA GGT TTG CCC CCA GTC
 Exon 6 Ile Ser Val Ser Gly Gly Gly Leu Pro Pro Val
 Ser Thr Leu Thr Asn Ile His Ser Leu Ser His Asn Pro Gln Ser Gln Asn Leu Ile Met Thr Pro Leu Ser Gly Val Met Ala
 AGC ACC TTG ACG AAT ATC CAC AGC CTC TCC CAC CAT AAT CCC CAG CAA TCT CAA AAC CTC ATC ATG ACA CCC CTC TCT GGA GTC ATG GCA
 447
 Ile Ala Gln S(er)
 ATT GCA CAA A GTAAGTTCTATTCTTGGTTGGAAACCTGGGGCAGGAGAGAATGGGAAGCAAAATTAATGTGTGTAATAAATAACTGTAGGTCTCTTCAAACTCACCACAAAC
 EX6R
 TAGTAAATTTGGTTTAACTCTTTAGTTTCTATCTCTCTCTCTTAAATCCCAATATTTGGATTTGATTTAGCCTTAAACAAAGAAAAATTTGTGGATTTGGATCTCTGGTCACAGTTTACG
 AGCTGTCATCCTGGGTCAAATCATTTGAACCT:.....4 kb :.....ATGACTCTGGGAGACTCTCAGGCTTTTAAATCAGATCTGTTTAAATGCCCATCTCCAAACCCACAACTCATTTG

FIG. 27F

TGGAACTTGAGCAAGTAAATTAATATCTCCCAAGTCTCGGTTTCTTTACACTTGGCTCCCATGGGAATCTCTATGTAAACAGGCTCAGCCCGGTGACTGGGACATTTAGCCGGGGGCTCAAATG
 447
 ATGGCATCCATCCACCTCTCCTTATCCAGGAGCTGTCTGTCTCTTTTCCCTCTGCTCCACAG GC CTC AAC ACC TCC CAA GCA CAG AGT GTC CCT GTC ATC AAC
 Exon 7 (S)er Leu Asn Thr Ser Gln Ala Gln Ser Val Pro Val Ile Asn
 Ser Val Ala Gly Ser Leu Ala Ala Leu Gln Pro Val Gln Phe Ser Gln Gln Leu His Ser Pro His Gln Gln Pro Leu Met Gln Gln Ser
 AGT GTG GCC GGC AGC CTG GCA GCC CTG CAG CCC GTC CAG TTC TCC CAG CAG CTG CAC AGC CCT CAC CAG CAG CCC CTC ATG CAG CAG AGC
 512
 Pro Gly Ser His Met Ala Gln Gln Pro Phe Met Ala Ala Val Thr Gln Leu Asn Ser His M(et)
 CCA GGC AGC CAC ATG GCC CAG CAG CCC TTC ATG GCA GCT GTG ACT CAG CTG CAG AAC TCA CAC A GTAAGGACACGGGCATGTGGAGGGAGGGAGCACTCA
 EX7R
 GGACCTCAGTGGCCAACCACTTTCCCTCTCTGGGCTCTGAACCTTCTCGGAAGTTTATTGGCTTGTGTCACCTTTCCCTGCTATGATCAACCGACTAGACAAATTTCTCAAGCATAACTCT
 TGAGTGTGCTGTACCTTTTCTAGTCCCTTCTCTACCCCTGAGATTCCAGGGAAGGTTTGAA::: 2 kb ::::: TGACCTTTGCTCCCGTTCCGTACCGGAGGCCCTCCCT
 GGTAGGAAATGTGTCTGAGAGCAGGTGGTTCTCCCTCAGAGCCCAAGCATCCACATGCTTTTCGGAGTTGGTTATGTGACTTGGAAATTTACATGAATCTTATGGATAACTAATATAGAGAA
 EX8F
 ATCCCCACTATAACCAACCAAGCCCTTTTATCTACCTGAGGAGATGGGAGCTATGGTGTGGGATGGGGGCTCTGTACCTGTGTCTTTCCCTGTGTATGCACCTTGATTTCTGTCTTCTCTGT

FIG. 27G

GCGGAAAGCCAGTTCCCTCTATGCAATATGCCCAATGCGCTCTCCACAGATGTCAGGACTCCTGTCTGTGGAGGTGGAGACAAAGGAACCCAGAGAGAGCAAGAAAGCC
 GTACTGTCTATGTTGTGATCCTTCATCGAACAAACTGATGCGAACTTGAACTCTGTCTACCTGAAATGAGGAGAGAGGACATGTGCTATTGAACTGAGCCCAACACACTGTAAATATCCAC
 AGACTCCCTCCCTGCCCTGCCCATCCACATGATCTTTGAGATTTCTTTTAAAGAAATTTTGTCCAAATGGCTGTAAACTATAAACTACTGTAAATTAAGTGCAATTTCCCTCTGTGTCTC
 TCCCTCTGCCCTGTATATACTAAAGTGTCTATTAGTTTCTTTTGTAAAGTCAGAGTCAAAATTTCAAAGTGTCTGTCCCTCTCCCTCATGGAGAAACATCCTAAAGTGGAAAG
 TGAAGCCCTTGTCTCTCCCGGGCTGGACACTTATGGGACAGCATACCTTGGACTGACTACAGCTAACTCCAGTCTCCTGACATTAGACACACACTCTCTGGATCCCTGGAGGGGC
 CTCAAAAGCCCTTCATTAACCAATTTATTTATCACTAAAAAAA
 TGAATGTAGTGTGTCAGAGTACATGCCAGCTTCCTGTGGCCAGGAGCTCAGCTGCACCTTAAGAAACCCAGGGCAGGAACTGGCTGTTTGTATAGCAGAGAGAAAAAGTTGCAGT

FIG. 27I

1 TGGGTTGCCCTGTGACTGCACCTGGCGATACCCCCACAAGCCCACCTCTGAAGGTAGAGACGGGTGGAGAGAAACAGGGGGATGCAAGGGG

91 GGATACGAAACACAGGAGAGGAGGAGGGGGAAGAGGATGGACGCTACACAGSCCCACTTGGTGCTTGTATTATGCCCATCTCATTTCCCTT

181 CTCAAACCAACCCCTTTGAAGTTGATTGTACATTTTACAGAAAGGAAACTAGGCTCGGAGAGGAGAAATCATTTTACCAAGGTCCTCCAGTTA

271 GTAGACGGTAGGTGCTGAAATGTAAATCCAGGTCTCTGCCCTGCTCCGGAGGGGGTGGGGTGAGGGAACACAGGAGAATGTGATGGGAAA

361 ATCCGAGATGGAGCCAGCCTGGGCCAGAAACACTGGGAGCTGTGGGAGACCGAGAGGGCAGGGTGGGATCACAGGAGCAGGAGCGGGG

451 AATTGGAGGTGAATCTGGCCCTCCCAAACTTCCAGTCCATTCTGCTCCAGGGGAACCGGAAACTGCCGGGGAACTGGAAAGGGAGCTCC

FIG. 28A

541 CAGAACAAGGATCCAGAAGATTGGCATCTGGGGCTGGGATTAGGTTTCTAAATCGTGGGCCATGGGCAGCCTTATCTCTGCAAAAGC
631 ATTGAGGGGTAGAAATCAATGATTTGGGAGTTATTGAAATTAGGGGATCTCGGAGGTAGGCTGTCAAGTGCCTGATAGTATATCAGTTAGAATG
721 CCTGACTTGGGGTGACAAATGGCTTGGAGGGGTGGTGAGTCAAGGGTCAAAATGAGTGCCTCGTGAATCATGATGCGCTCTGTTGTAACAATTG
811 ATAACTGAACATCGGTGAGTTAGGGCCCCAGCAGTTGTAAATTAGCACCCCCGGTGTCAGCCAGAAACCAACAAACGAGCCAAATCCCTCGCA
901 GCCCGGCCAGCCTATCCACCGCGGGGGACCGATTAACGATTAACCCCCACCCTCCCCGGCAGAGCCTCCACCCCTTCACAGAGGGCTA
991 GGCCAAGACTCCACAGATCTTCCACAGGACGGTTTGAAGGAAGGCAGAGAGCGCACTGGAGAGGAGGCAGTGGAGGGCGGAGGGCGG

FIG. 28B

1081 GGGCCCTTCGGGTGGCGCCAGGTAGGCGGGCGGTGGAGGAGGAGATGCCACTCTCCAAAACCCCTCGTCGACATG
 AspMetAlaAspTyrSerAlaAlaLeuAspProAlaTyrThrLeuGluPheGluAsnValGlnValLeuThrMetGlyAsnG(1y)³⁰
 1171 GACATGGCCGACTACAGTCTGCACTGGACCCAGCCTACACCCCTGGAAATTGAGAATTGTCAGGTGTTGACGATGGGCAATG GTAGG
 1261 TGGGGGCAGATGTGCCCAGGTGTGCCAGTGGGGGCAGGTGTGCTGGGTCCAGGAGCAGATCTTTGGCACTCAACTTTGGGGTGGGAGGA
 1351 GAATGATACAAAAATGGTAGGTTGGTCTCTACAGGCCAGCACAGGTGTTGCCAAGTGAAGCCCATGTGCCAGGCCACAGTGATCACAGGCCAT
 1441 TCTGGGTGAAGGAGGCCCTGCAAGGGCCAATTTCAGCAAAAGTCGATCCCGGCTATTCTCCACAG GCCCTTCCAGTCCCTCACTGCCTCA
 Exon 1C (G)lyProSerSerProHisCysLeuT
 A

FIG. 28C

[illegible]

FIG. 28D

2071 CATAGAGCACATGCGTTTGTGCAATGCGGACCTGTGGAGTGCCTCTCTCTCGCATCTTATCCGTATGCGCGTTTGTGCTGTGCCC
 E1BF
 2161 CATATTGTACCTGCTGTGTATATATGCAGTTCCCTGTGCTGCGGGCGGGGTCAACGGTCTCTGTGTGCACGACTGCACAGACCCAAA
 A
 2251 TGCAGGACTCTGTGTTGCCACTCACCAAGTGAGATTATATACACCAACATGTCCGTTTGTCTCTGTGAGCAG ATTTGTGTCGCGCTGCGTC
 Exon 1B IleLeuLeuProLeuArgL
 euAlaArgLeuArgHisProLeuArgHisHisTrpSerIleSerGlyGlyValAspSerSerProGlnGlyA(sp)
 2341 TCGCCAGATTGAGGCATCCCTCCGACATCACTGGAGCATATCTGGAGGGGTGGACAGTTCTCCACAGGGAG GTAGGGGAAAAAGAGGAGG
 G

FIG. 28E

2431 CCCGAAACCCCTCCTGGAGGGAAGAGCCCCCATCGGTCCAGGCCAGCCTCAGAGAGAGGGGCGACGAGCTGGCTGAGGTCAGCCTGC
 2521 CACCCCTGCTTCTTCTGTGTCTTGGAGCCACTCAGCCAGTATGAGGCTGCAGCTCCAGCTGAGGTCTGGAATCTTGTGGTCAGCTCAGCT
 2611 AGGGTGAGGAGGCAGCTGCTGGGCACTGCTTGTGTCAGCTCAGCAGGTGCTCACCTGCCCTGCCCTCAGTCACGTGTGACCTTGGGC
 2701 ATGTCACCTCCCCATCCTGGCTTCTGTATCTTCTACAAACAGGCTTTCATCCCCCAGGCTGCTGGCTGGACGGCTTTAGGCCTGTC
 2791 TGAGGACCAACGCCAGGAGCGCAAGGCAAAACACACCAGAGAT::: 4.4 kb :::::CCCCTTGGGAGTTAGGAGGGCGGCTCC
 2881 CACCCAGAGGTGGCCAGGTTTTCATGCCCTTCTAGAGAAAGCTGGGCTGGTGGCTCCACCACAGGGAGACGCAGACCCCTCAGAAAC
 2971 AAGTCTGTGAAGTCACAAACAGCCCGAGTTTACAGATGTGAACTGAAGCTCCAAAGTCAGGAGGTCACTCAGTGGGAGGTGATGGA

FIG. 28F

3061 GTGGGAACAGCCCCAGATCTGGCTGAGCGCGAAGCCCTGGAGAGATCCCCGCAAGGCTCCCTTAGATGGCTGACATTCTGCTCTTCTCCTG
 E2F →
 3071
 3081
 3091
 3101
 3111
 3121
 3131
 3141
 3151 AAGCCTACTCCCTTCTCTCTCTGGGGCAG ACACGTCCCCATCAGAAGGCACCAACCTCAACGCGCCCAACAGCCTGGGTGTGACGCGCCT
 Exon 2 30
 3161
 3171
 3181
 3191
 3201
 3211
 3221
 3231
 3241 uCysAlaIleCysGlyAspArgAlaThrGlyLysHisTyrGlyAlaSerSerCysAspGlyCysLysGlyPhePheArgArgSerValArg
 GTGTCCATCTCGGGGACCGGGCCACGGGCAACACATACGTGTCCCTCGAGCTGTGACGGCTGCAAGGGCTTCTTCCGAGGAGGACGTGCG.
 3251
 3261
 3271
 3281
 3291
 3301
 3311 gLysAsnHisMetTyrSerCysArg (g)
 GAAGAACCAACATGTACTCCTGCAG GTGAGGAGCCCTCAATTCTTCACTTGGGAAATGGGCACACTTGGGCTCATGSGCCCCCAAGGTCTGTGTC
 →→ E2R
 3321
 3331
 3341
 3351
 3361
 3371
 3381
 3391
 3401
 3411
 3421 TTCTCCCTCAGTGGGTAGGTCACAGACAGCTGCCCTTACGGGGCCCTCAAGGCTCTTCTGGTTTGTATAAAGACTTTGTGTAATCCCAAGA

FIG. 28G

3511 AGAGCATCTATTCTAGGAACACACATTTACTGATCATCAAGCTACTGGCTGCCGTTTATTGAGCTCTTATCATATGCCAGGCACAATACTA
 3601 AGTCTTTTGTGTATTAC::: 1.6 kb :::::GTACTCCAGAGGTCAAGGTTCCCAACTCAGCTCTAACACCAACCAGCAGAG
 3691 CGACCCAGGACCAACATGTTGCCTCTCTGAGCCTCAGTTTCCCATGTTTAGCAGGACAGGACTGGGCTCTTAGAGAGTTTCATAGCACCTT
 3781 TCCAGCTCCTGGTGGGTTCAAGAGAGAACTCCCGGGATGAAGAGATGAGACACTGAGGTTGGGGGGTCAACTGGATAGCCAGGGGCCCTA
 3871 GTTCTCTCCTAAGAGAGGAGGAAGTTGTGTCTTCTCCATCCAAACCATCCAAAGCCCTCCCCAG ATTTAGCCCGCAGTCCGTGGTGGACAAAG,
 E3F →
 Exon 3⁸⁸ (Ar)gPheSerArgGlnCysValValAspLysA

FIG. 28H

3961 sDLYsArgAsnGlnCysArgTyxCysArgLeuLysLysCysPheArgAlaGlyMetLysLysGluA(1a)¹²⁰
 4051 ACAAGAGGAACCAAGTCCCGCTACTGCAGGCTCAAGAAATGCTTCGGGCTGGCATGAAGAAGAAG GTGAGCCTCGGCCCTCCCCGCCCC
 4141 ACCACCACTGCCCCACCTGCACCCACAGCTCCCCGACAGTCATTACAAGTGTAGCCACACTTTATGACTCAGTGGCAGGCCCCAGGGTG
 4231 ACTGGCTAATGGCTGAGAAGAGGGGCGCTGGAATCTGACCATAGGAGCGGCTGGCTTGGTCTTGAGAAAGATTC::: E3R
 5.9 kb ::TCCCACCTCCTCATCAGTCACAGACACCCCAACCCCTACTCCATCCCTGTTCTCCCTCCTCACCTCTCTGTGCTCCTCAC
 E4F
 Exon 4

FIG. 28I

120
 (A) laValGlnAsnGluArgAspArgIleSerThrArgArgSerSerTyrGluAspSerSerLeuPheSerIleAsnAlaLeuLeuGlnAl
 4321 AG CCGTCCAGAAATGAGCGGGACCGGATCAGCACCTCGAAGGTCAAGCTATGAGGACAGAGCCTGCCCTCCATCAATGCGCTCCTGCAGGC
 155 T(R127W) : (T/I130)
 agluValLeuSerArgGln
 4411 GGAGGTCTGTCCCGACAG GTACCGGGGTGATCTGCCACCCACCCAGGGATCCCCCACACTACAGAGGAGCTCACCTCCTCCACCTCCA
 4501 TTCTCCCCAGCCAGGCCCTGGAGCAGCTGACGGGAGGGCCCTCAGATATTACAGAGGGACACTGAGTGGGTTTCACATGGGCCCCAGTTT
 ← E4R
 4591 GCAGCAAGGGCAGGAATCGAACTGGCGGCCCTGGGGCACTTTCTAATTCTATCTGCTGCTGCCACAGGCCCAAGCAGAGTCTTCAC
 4681 CTTCACTGAGGGCCTGCCATCAGCTCAGTCCGAGAGAACAGAGCAGTGGCTCAGTGGAGAGAGGTGGCAAAGTGGGGCCCCAGCCCTTCC

FIG. 28J

4771 CTTGCTGAGTGACCTTGGGCAAGTCACAGCACCTCTCTGAGCCATGGTTGCCCTCATGTCAGAAAAGGATGATGATTTTGGCCCTGCCTT
 4861 CTCCTCTAAGGCTGACAGACTCCTTGGGGCTCTAAAGCTG::: 1.0 kb :::::TTCTCCCTCATCCCTGCCTCCTCCCTCCCT
 4951 CCGTTTTTACCCTGAGCTTCTTCAGAGCTGGAGGGCACCCACTATCCAGCCCCCTCCCCACATCTGATTCACAGGAGGGGGCTCTGTGC
 5041 AGGGGACAGAGATGCGGGAGGGGGCGGACATCTCCAGCATTTTCTCCCTGTATCTCTCGAAG ATCACCTCCCCCGTCTCCGGGATCAA
 E5F → Exon 5 156 IleThrSerProValSerGlyIleAs
 nGlyAspIleArgAlaLysLysIleAlaSerIleAlaAspValCysGluSerMetLysGluGlnLeuLeuValGluTrpAlaLy
 5131 CCGCGACATTCGGGCGAAGAAGATTGCCAGCATCGCAGATGTGTGAGTCCATGAAGAGCAGCTGCTGTTCTCTCGTTGAGTGGGCCAA

FIG. 28K

sTyrIleProAlaPheCysGluLeuProLeuAspGln¹⁹⁷
 5221 GTACATCCCAGCTTCTGCGAGCTCCCCCTGGACGACCAG GTGAGGATGGCGGTGGATGGTGGCAGTAGTGGCAGTGGCGGGGCGAGC
 5311 CAGGGGGCTGCTGGCCACCTGGGATATAGCCCGTGGACTGGCTTGATTTTATTTTAAACAAATATGTAGTGCACACACGTTGTCTGA
 5401 AACTTTAAATCACCCTTACAAATATTAACTCAGTTAGCTCCTCCAAACAACCTCTATGAGGTAGGTACTAAGGTACTATTATTACTGCCATCT
 5491 CATAGGTGAGGAGATTGGGGGCACAGAGAGGTTAAGTAACCTGCTCAAGGTCACATAGCTACTATCCAGCATAGCTGGG::: 4.3 kb
 5581 :::::::ATTTTACAAAGCACCCCTTCATAATTCTCCATAGCTGGTCCATGGGTGGAAATTGCGGACCCACAGTTTGGAACTTTTGG
 5671 GATCATAGACCTTTTTCAGAAATCTCAAAAAGAAAAAAGCACACAGAAATGTTGCTTACAGTTTCAATCAGGCGACACAGAGAGGCCCA
 5761 GCACGAAGCAGTTTCTTGCCCAAGGACACAGCAGTTCAAGGACAGAGTCAGCGGAGGTCTCTCAGCTCTGAGCACATGTTCTTTCCCT

FIG. 28L

5851 TCCAGGTTTCTAGTTTATGGGTAGTAGTTTATGATGCCCATTTACAGTTCAGGCAGGTAGAGGAGGGAGCATTAAAGCTGACTT
 5941 GCCCAGCGTCACTGAGTTGGCTACGGGCAGCCTTCCCAAGGTACAGATGGCAACACTGTTCCTTCTCTTTTCAG GTGGCCCTGCTCA ValAlaLeuLeuA
 6031 rgAlaHisAlaGlyGluHisLeuLeuLeuGlyAlaThrLysArgSerMetValPheLysAspValLeuLeuG (ly) Exon 6 198
 6121 GAGCCCATGCTGGCGAGCACCTGCTGCTCGGAGCCACCAGAGATCCATGGTGTTCAGGACGTGCTCCTAG GTGAGGCGGCTGCCT
 6211 GCCCTGGCCAGGGCTCCAGGGAGGGTATGCCCTAGCATGGCCTCACCCAGGCAAGGAGATTACATGGTGGCATGCCAAGGGTGAGGGAGA
 6301 CTAGTCAGGAGTGGCCCTGTCTCAGGCTTGCAATGGAGGGCTCCAGGACTCAGTTTTCAACTGGGTACCCCACTCAGATGCCAAGGAAAT
 GTGATGCAAGTCACCAAAATTCCAGCAATTGAAGTCAGAGCACGATCAGGGTTATCCCTGGAAATTACCTGTGCATCCTTTTCTTTTGA

FIG. 28M

6391 CAGAGTCTTGCTGTCACTCAGGCTGGAGTGCAATGATGTA: : : : : 1.4 kb : : : : : GCAAAACACTACCTATTTTAATATAACA
6481 ATGCTATGAGGGAGCTCGATTATTTATCCTCATCTTATAGATAAGAAAACTGAGGCACAGAGAGGTTAAGTAACTTATCCAACTATAACC
6571 AGCTATCAGGGGCAGAGGCCATTAAAGCAGGCGAGTGCAGTTCAGAAATCTGGTCCCTTAACTTATGATGCTTTTGGTGCCCTATCAGGTGACC
6661 TTTGAATGTCATCGATCTTGTGAGTCATGTTGGTAAATGAGAGCTTGGGTGATGTGAAAGAGGTCCTAGAAAGCCAAAGTTCCAAAGCTCAGC
6751 CGGATGACTCAAGGCAGCTTATCTTCTGAAATCTGGGCCCTCAGCTTCCTTACCTGTGAAATGGGAGTCAACCATCCCTGCAGGTCTCTCTCC
6841 CACAGGCACCAGCTATCTTSCCACTTAAAGCCAAACTAGAGGAGAGGGGTCAACCCAAAGGTGACTTCCCATTCCTCCCTCCCTCCCAA
E7F →

FIG. 28N

237
 Exon 7 (G)lyAsnAspTyrIleValProArgHisCysProGluLeuAlaGluMetSerArgValSerIleArgIleLeuAspGluLeuV
 6931 CCCTTCCAG GCAATGACTACATTGTCCCTCGCACTGCCGAGCTGGCGAGATGAGCCGGGTGCCATACGCATCCTTGACGAGCTGG
 allLeuProPheGlnGluLeuGlnIleAspAspAsnGluTyrAlaTyrLeuLysAlaIleIlePhePheAspProA(sp)
 7021 TGCTGCCCTTCCAGGAGCTGCAGATCGATGACAAATGAGTATGCCCTACCTCAAGCCCATCATCTTCTTTGACCCAG GTACAGTGCACACCT
 T(Q268X) C
 7111 CCTAAGCCATCCCTGACTCTCTCTCCAGAACGCTCTGCGAGACTTCTCTTATTGGGTCTGTACACTGAGTTCACAGCCCTCATCTCATGT
 E/R
 7201 TAACGACAGCCAGGAGAGGCCGTTTTCATTTAACAGATGAGGCAAGTCAAGATTGAAAGAGACAAATATGGCCGGGCGCAGTGGCTCACAC
 7291 CTGTAATCCCATCACTTTGGGAGGCTGAGGCGGCGGATCACCTGAGGTCAAGGTCAAGATGAGCCCTGGCTAATGAGAAACCCCAT

FIG. 280

7381 CTCTACTTAAAA::: 1.5 kb ::::GTGGCTCTGCCAACAACCTGGCTGTGGACCCAGGACAAGTCCCTATCTTTGCACGTGTGT
7471 CTGGGTTTCCCGGTGTGAAGATGAGGCGGTTGCTAGGTGCTTATTGGATGCAATTCCTCAAGTCCCGCCCTCCATCTCCTATTCCCTCT
7561 CTTCTGGTTTAGTGCTTTAGGAAATGTGCAGAAAATCTTTTCTGCCCTGTGTCTAGGAAATCATAATTCAATGCTGGCGTACCCCTGCTGTGT
7651 TGAGTCCCCTGAATCCCTTGTGCCCACACTGCTGAAGACTCCCTTGTGTGACACACAAGTCAAGGGGACATCTGGGTCTTGACTCCCCCAGATGCT
Exon 8 289 (A) spAlaLysGlyLeuSerAspProGlyLysIleLysArgLeuAr
7741 CCAGCTGGACCCCTGCTGCCCTCCCTTGCCACCCCTCTTCCATTGTAG ATGCCAAGGGGCTGAGCGATCCAGGGAAGATCAAGCGGCTGCG

FIG. 28P

7831 gSerGlnValGlnValSerLeuGluAspTyrIleAsnAspArgGlnTyrAspSerArgGlyArgPheGlyGluLeuLeuLeuLeuPr
 TTCCACGGTGCAGGTGAGCTTGGAGGACTACATCAACGACCGCCAGTATGACTCGGTGGCCGCTTTGGAGAGCTGCTGCTGCTGCC

7921 oThrLeuGluSerIleThrTrpGlnMetIleGluGlnIleGlnPheIleLeuPheGlyMetAlaLysIleAsnLeuLeuGlnG1
 CACCTTGCAGAGCATCACCTGGCGAGATGATCGAGCAGATCCAGTTTCATCAAGCTCTTCGGCATGGCCAAGATTGACACACCTGTTGCAGGA

368
 uMetLeuLeuGlyG(ly)
 8011 GATGCTGCTGGGAG GTCCTGTCACCAAGCCAGGAGGGGGGGTGGAGTGGGGACTCCCGAGGAGACAGGCCCTCACACAGTGCACACC
 G P C Q A Q E G R G W S G D S P G D R P H T V S S P

8101 CCTCAGCTCCTTGGCTTCCCCACTGTGTGCCGCTTTGGCAAGTTGCTTAACCTGTCTGTGCCCTCAGTTTCCTCACCCAGAAAAATGGGAACA
 L S S L A S P L C R F G Q V A

FIG. 28Q

8191 AGGCAATGGTCTATTTGTTTCAGGCACCGAGAACTAGACGCTGCCAGTCACTGTTCTTAAGTGTGGCAATTCAGCAAGACAAGATCTTT
 8281 TGCCCTCGGGGAGGCTGTGTGTGTGAGTATGTATGGATGCGTGGATATCTGTGTATATGCCCGTATGTGCGTGCATGTGTATATAAAG
 8371 CCTCACATTTTATGATTTTGAATATAACAGGTAATATGA::: 4.4 kb :::::GGACACATAGATGCTATAAGTAGGTCAGTT
 8461 GGCTGCACAGAGATGTGGGGGATGAGGCTGAAAGGTGAGCGGGACCAAAATGGTTGAAAGGACTTGCACCTCCAGAGAGCTTTGAGAGCCCA
 8551 TTGATTACATCCATTATGTTACTATGTGACCAATACATTACTCATTAGAACAATTTACGTGATCTCAGAGCTTCCCTTATATATGCACCTTGTT

FIG. 28R

8641 CCTTCAACTCACTTTGTCTCTTGGTTTGGGGTCTCTTAAACACCTCATGAAGTCTATAGATGGGAATGGTACACCTAGTTTA
8731 CTAACCCAGGAATAGGTACCCAACAGGCACTGCCAATATTGGATGGGCTGGTTGATTTGGCCACGCCCTGAGGAAGATGGCGTCCCAAGGCC
8821 TGAGGTCTGCATCCAGACTCTCCATCCTGATCGACCTTCTCTACCTGCAG GTTCCCCAGCGATGCACCCCATGCCACACCCCTGC
Exon 9 368
(G) lyserProSerAspAlaProHisAlaHisProLeuH
isProHisLeuMetGlnGluHisMetGlyThrAsnValIleValAlaAsnThrMetProThrHisLeuSerAsnGlyGlnMetCysGluT
8911 ACCCTCACCTGATGCAGGAACATATGGGAACCAACGTCATCGTTGCCAACACAATGCCCACTCACCTCAGCAACGGACAGATGTGTGAGT
419
xpProArgProArgGlyGlnAlaA(1a)
9001 GGCCCCGACCCAGGGACAGGCAG GTGGGCAAACTCTGGGATTTTACCTTGCAAGGGTGAGGATGGGCTTAAGACAGGAGGCAGGAGA

FIG. 28S

9091 AAGTGGAGTCTAGAAAGGTAGAACCCAGGATCCAAACAGTTTCTCTGGGTTCCAGGGTAGGGATAAAGGGCAAGATTGTCCATTGTGTGAGGC
 9181 TGTATTATTCAGTAAGGTGACTGACAGCCCTTTACTGAATGAAGCCATTGTGGGATGAGGCAATCCCACTGGATGAGGTAACCCATTGGGTG
 9271 AAGATGCTCTTGGGTGAGAAATCCCATTTAGTTGACATTGTCCATTAAAGTAAAGTAAAGGCTGCACAGTTGGGTAAGGCTA
 9361 TCCATTAGACATTAGATGAGACTACCCATTGGGTCAGGATGTCTGCTGGGCTA::: 1.4 kb ::::TTTGGGAGAACAGTCC
 9451 AAGTCTGCATATCAAAATAAATGATGGAGAGATGGGTGGTAGGACCTTCCAGACCTCATAAACTTAGGCTTTATGATCTGGGACTCACA

FIG. 28T

9541 GAAGTTGAGCAATAAAGACCTTAGGGATTATCTGGCTTAATTAATCTCTCATTTTATAGAGGAAGAATTAAAGTCAAGGTGGGGCAG

9631 GGTGGAGGGGAGAACTTTCCCGGGGCTCTTCATTACTCCCAAGGCTGGAATTTTGAGCAGCCCCCTGCTGTCTGTTTGTCTTCC
 419 Exon 10
 (A) laThrProGluThrProGlnProSerProProGlyGlySerGlySerGluProTyLysLeuLeuProGlyAlaValAlaThrIleVa
 9721 AG CCACCCCTGAGACCCCAAGCCCTCAGCCAGGTGGCTCAGGCTGTGAGCCCTATAAGCTCTGCCGGGAGCCGTCGCCACAATCGT
 lLysProLeuSerAlaIleProGlnProThrIleThrLysGlnGluValIleOP 465
 9811 CAAAGCCCTCTCTGCCATCCCCCAGCGACCATCACCAAGCAGGAAGTTATCTAGCAAGCCGCTGGGGCTTGGGGGCTCCACTGGGCTCCC

FIG. 28U

9901 CCCAGCCCCCTAAGAGAGACCTGGTGATCAGTGTACGGCAAGGAAGACGTGATGCCAGGACCAGTCCCAGAGCGAGGAATGGGAAG
 9991 GATGAAGGGCCCCGAGAACATGGCCCTAAGGCACATCCCACCTGCACCTGACGCCCTGCTCTGATAACAAGACTTTGACTTTGGGGAGACCCCT
 10081 CTACTGCCCTTGGACAACTTCTCATGTGTGAAGCCACTGCCCTTCACTTCACTTCATGCCATGTCCAACCCCCGACTTTCATCCCAAAGGAC
 10171 AGCCGCCCTGGAGATGACTTGAGCCTTAC

FIG. 28V